

1/28

Sal I Bam H I

| |  
----- pUC 19

Xba I

1 ATGGAGTCAA AGTTTGCTCA CATCATTGTT TTCTTCTTC TTGCAACTTC  
original sequence - ag a  
51 CTTTGA~~AA~~CT CTCTGGCAC GAAAAGAAAG Tgatggacca gagatcttaq  
mutagenic primer  
101 aacTTCAAAA GGAATTGAA TGCAATGGAA AACAAAGGTG GCCAGAACCTT  
151 ATTGGTGTAC CAACAAAGCT TGCTAAGGGG ATAATTGAGA AGGAAAATTC  
201 ACTCATAACT AATGTTCAGA TACTACTGAA TGGTTCTCCA GTCACAATGG  
251 ATTATCGTTG TAATCGAGTT CGTCTTTTG ATAACATTTT GGGTGATGTT  
301 GTACAAATTG CTAGGGTGGC TTAA

**Figure 1**

1 GAATTCCGCA AGGAgcacac ccggctgtcc acctgCTGCA GAGATGGTGC  
upstream primer  
51 ACGCAACCTC CCCGCTGCTG CTGCTGCTGC TGCTCAGCCT GGCTCTGGTq  
cc t original sequence  
101 gctcccgga tccctgccag AAAGTGCTCG CTGACTGGGA AATGGACCAA  
mutagenic primer  
151 CGATCTGGGC TCCAACATGA CCATCGGGGC TGTGAACAGC AGAGGTGAAT  
201 TCACAGGCAC CTACATCACA GCCGTAACAG CCACATCAAA TGAGATCAAA  
251 GAGTCACCAC TGCATGGAC ACAAAACACC ATCAACAAGA GGACCCAGCC  
301 CACCTTGCG TTCACCGTCA ATTGGAAGTT TTCAGAGTCC ACCACTGTCT  
351 TCACGGGCCA GTGCTTCATA GACAGGAATG GGAAGGAGGT CCTGAAGACC  
401 ATGTGGCTGC TGCAGTCAAG TGTAAATGAC ATTGGTGATG ACTGGAAAGC  
451 TACCAGGGTC GGCATCAACA TCTTCACTCG CCTGCGCACA CAGAAGGAGT  
501 GAGGATGGCC CCGCAAAGCC AGCAACAATG CCGGAGTGCT GACACTGCTT  
551 GTGATATTCC TCCCCAATAA AGCTTG  
+ Hind III

**Figure 2**

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SCT 10  
ECOR I  
↓  
1 GAATTCTGCAT ATGGCTGAAG CTGGTATCAC CGGTACTTGG TACAACCAGC  
51 TGGGGTCTAC CTTCATCGTT ACCGCTGGTG CTGACGGTGC ACTGACCGGT  
101 ACTTACGAAA GCGCTGTTGG TAACGCTGAA AGCCGTTATG TTCTGACCGG  
151 TCGTTACGAC TCTGCTCCGG CTACCGACGG TTCTGGTACT GCTCTGGGTT  
201 GGACCGTTGC TTGGAAAAAC AACTACCGTA ACGCTCACTC TGCTACCACC  
251 TGGTCTGGCC AGTACGTTGG TGGTCTGAA GCTCGTATCA ACACCCAGTG  
301 GCTGCTGACC TCTGGTACCA CCGAAGCTAA CGCTTGGAAA TCTACCCTGG  
351 TTGGTCACGA CACGTTCAACC AAAGTTAAC CGTCTGCTGC TTCTATCTAGA  
↑  
Xba I

Figure 3

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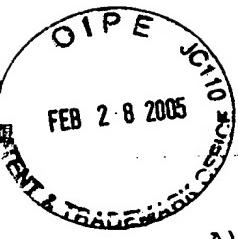
| |  
----- pUC 19

|  
Xba I

1 ATGGATGTTCAACAGGAAGT TAATTCGTT GCTTACCTAC TAATTGTTCT  
51 TGGTAAGATT TTCCCTTACT CCCTTGTTTT AAAAAATAAA AAAACAAAAA  
101 AAATCTTGGT TTTATACATAT ATATAACACAC AAAGTAGTTTT ATTTTTTTCC  
151 TTTATATTAT ATTTGTTGTA GGAATATTTC TACTTGTAG CGTGGTGGAA  
201 CATGTTGATG CGAAGATCTG TACTAAAGAA TGTGGTAATC TTGGGTTTGG  
251 GATATGCCCA CGTTCAGAAG GAAGTCCGAA AAATCCCATA TGCATCAATT  
301 GTTGCTCAGG CTATAAGGGT TGTAATTATT ATAGTGTGTTT CGGGAGATTT  
351 ATTTGCGAAG GAGAATCTGA CCTAAAAAAC CCAAAAGCTT GCCCCCTAAA  
401 TTGTGATACA AATATTGCCT ATTCAAGATG CCCCCATTCA GAAGGAAAAT  
451 CGCTAATTAA TCCCACCGGA TGTACCACAT GTTGCACAGG GTACAAGGGT  
501 TGCTACTATT TCGGTAAAAA TGGCAAGTTT GTATGCGAAG GAGAGAGTGA  
551 TGAACCCAAG GCAAATATGT ACCCTGCAAT GTGA

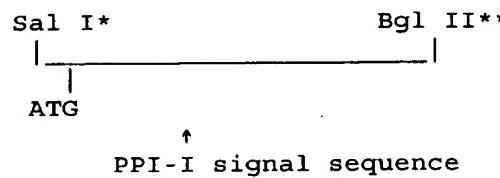
\* result of PCR error during isolation of the PPI-II sequence

Figure 4

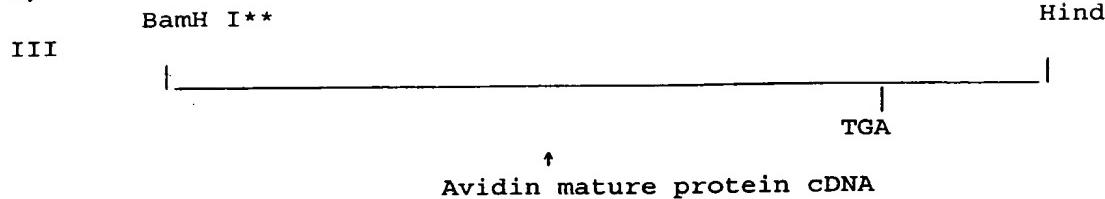


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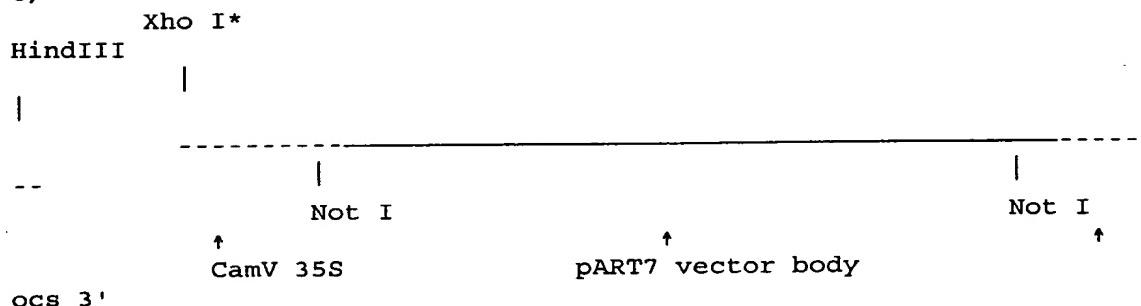
A)



B)



C)



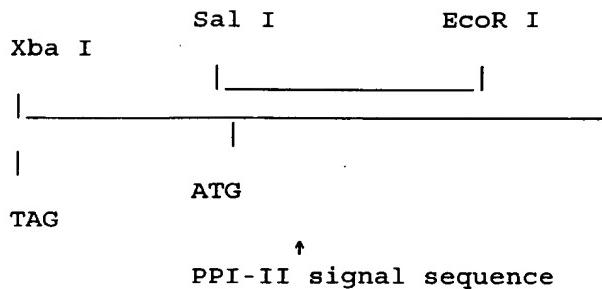
\* compatible cohesive ends  
 \*\* compatible cohesive ends

**Figure 5**

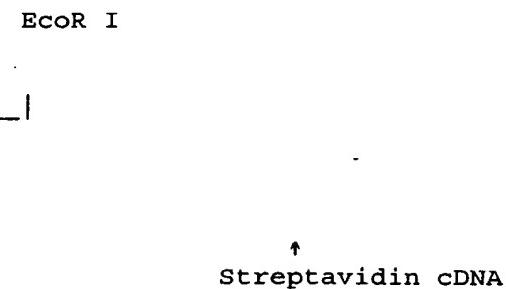
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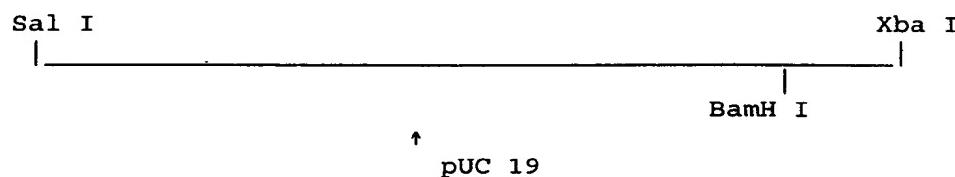
A)



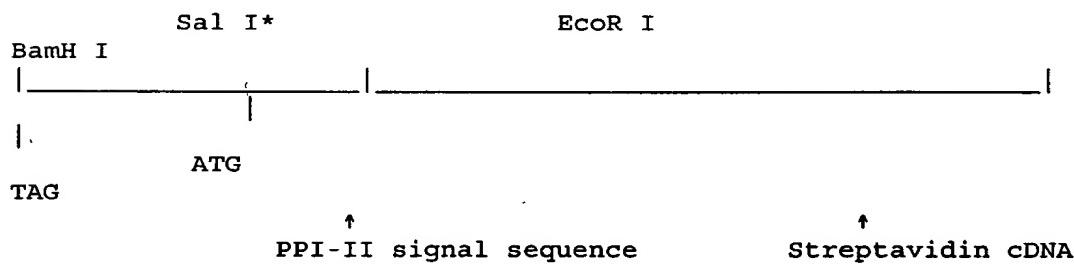
B)



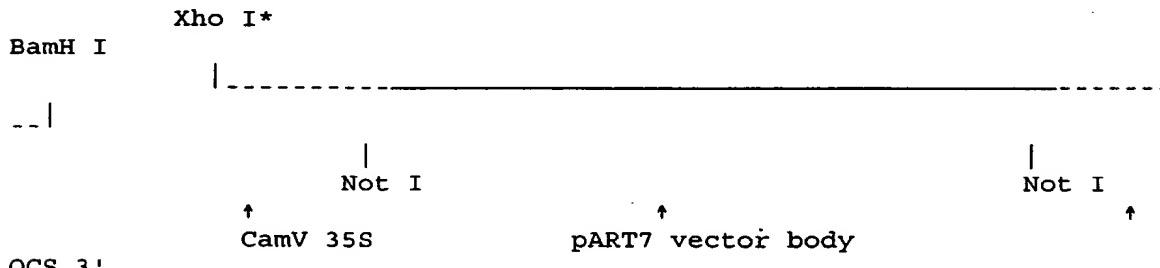
C)



D)



E)



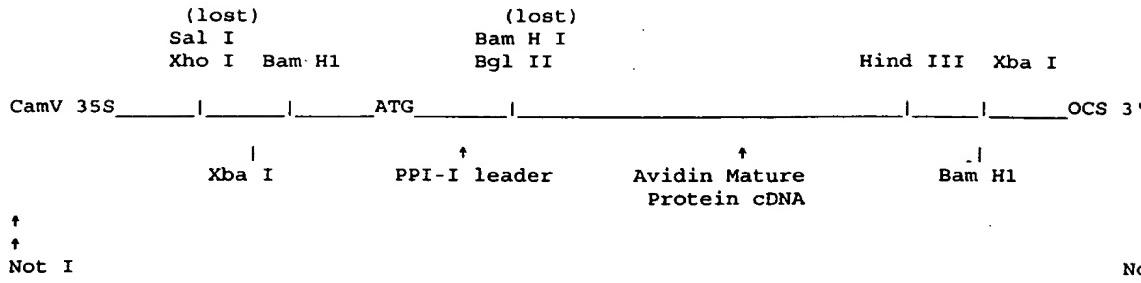
**Figure 6**

\*compatible cohesive ends

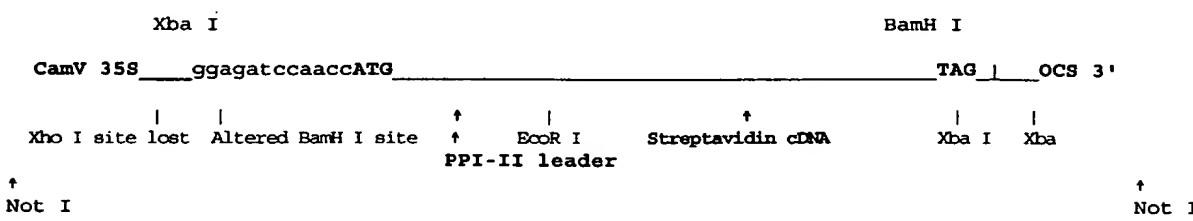


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A)



B)



**Figure 7**

A)

1 ATGGAGTCAGTTTGCTCA CATCATTGTT TTCTTCTTC TTGCAACTCC  
 51 CTTTGAAACT CTCTTGGCAC GAAAAGAAAG TGATGGACCA GAGATCCCTG  
 101 CCAGAAAGTG CTCGCTGACT GGGAAATGGA CCAACGATCT GGGCTCCAAC  
 151 ATGACCACATCG GGGCTGTGAA CAGCAGAGGT GAATTCACAG GCACCTACAT  
 201 CACAGCCGTA ACAGCCACAT CAAATGAGAT CAAAGAGTCAG CCATTGCATG  
 251 GGACACAAAAA CACCACAAAC AAGAGGACCC AGCCCACCTT TGGCTTCACC  
 301 GTCAATTGGA AGTTTCAGA GTCCACCACT GTCTTCACGG GCCAGTGCTT  
 351 CATAGACAGG AATGGGAAGG AGGTCTGAA GACCATGTGG CTGCTGCGGT  
 401 CAAGTGTAA TGACATTGGT GATGACTGGA AAGCTACCAAG GGTCGGCATC  
 451 AACATCTTCA CTCGCCTGCG CACACAGAAG GAGTGA

B)

cleavage site  
 ↓

1 MESKFAHIIIV FFLLATPFET LLARKESDGP EipARKCSLT GKWTNDLGSN  
 51 MTIGAVNSRG EFTGTYITAV TATSNEIKES PLHGTQNTIN KRTQPTFGFT  
 101 VNWKFSESTT VFTGQCFIDR NGKEVLKTMW LLRSSVNDIG DDWKATRVGI  
 151 NIFTRLRTQK E\*

**Figure 8**

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A)

1 ATGGATGTTCAAGGAAGT TAATTCGTT GCTTACCTAC TAATTGTTCT  
51 TGGTAAGATT TTCCTTACT CCTTTGTTT AAAAAATAAA AAAACAAAAA  
101 AAATCTTGGT TTATACATAT ATATACACAC AAGTAGTTT ATTGTTTCC  
151 TTTATATTAT ATTTGTTGTA GGAATATTTC TACTTGTTAG CGTGGTGGAA  
201 CATGTTGATG CGAAGATCTG TACTAAGAAT TCGCATATGG CTGAAGCTGG  
251 TATCACCGGT ACTTGGTACA ACCAGCTGGG GTCTACCTTC ATCGTTACCG  
301 CTGGTGCTGA CGGTGCCTG ACCGGTACTT ACGAAAGCGC TGTTGGTAAC  
351 GCTGAAAGCC GTTATGTTCT GACCGGTCGT TACGACTCTG CTCCGGCTAC  
401 CGACGGTTCT GGTACTGCTC TGGGTTGGAC CGTTGTTGG AAAAACAACT  
451 ACCGTAACGC TCACTCTGCT ACCACCTGGT CTGGCCAGTA CGTTGGTGGT  
501 GCTGAAGCTC GTATCAACAC CCAGTGGCTG CTGACCTCTG GTACCACCGA  
551 AGCTAACGCT TGGAAATCTA CCCTGGTTGG TCACNACACG TTCACCAAAG  
601 TTAAACCGTC TGCTGCTTCT ATCTAG

B)

cleavage site

↓

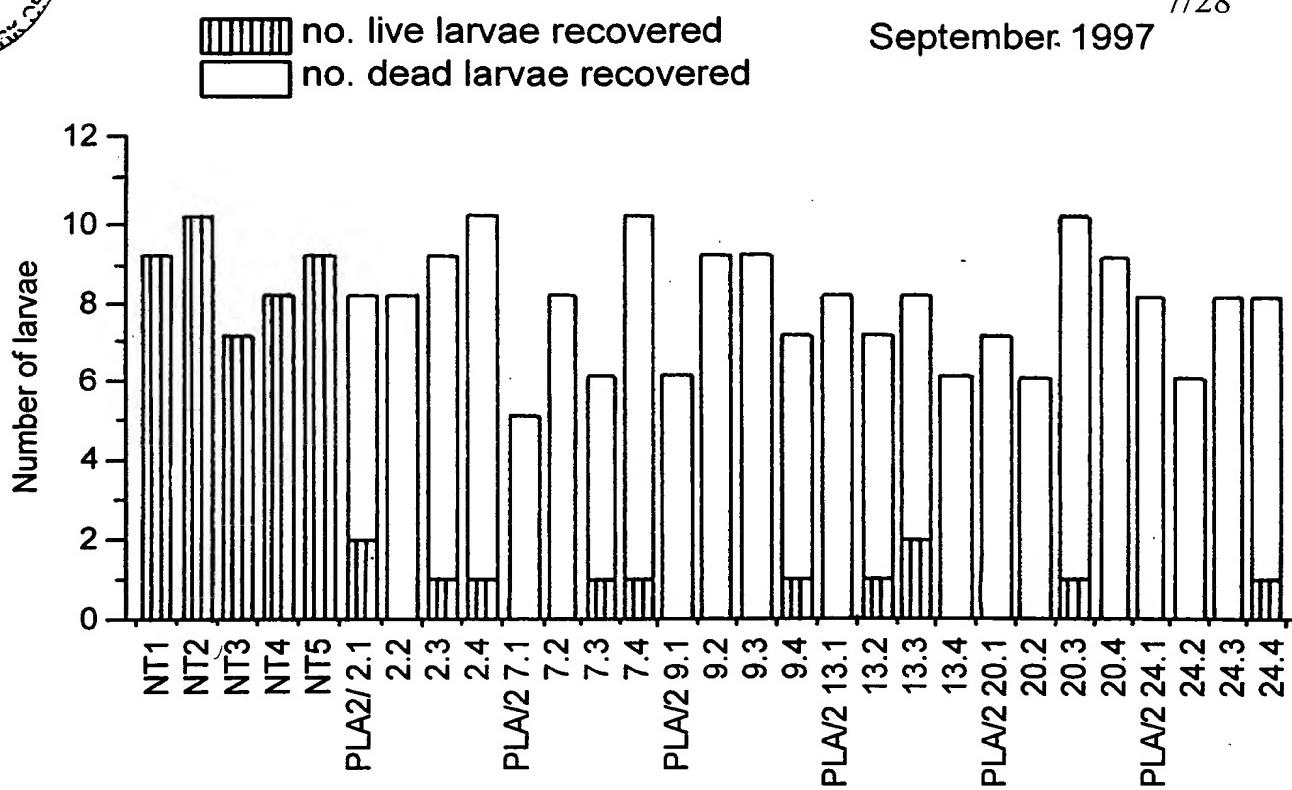
1 MDVHKEVNPFV AYLLIVLGF LLVSVVEHVD AKICTKnshM AEAGITGTWY  
51 NQLGSTFIVT AGADGALTGT YESAVGNAES RYVLTGRYDS APATDGSGTA  
101 LGWTVAWKNN YRNAHSATTW SGQYVGGAEEA RINTQWLTS GTTEANAWKS  
151 TLVGHDTFTK VKPSAASI\*

Figure 9

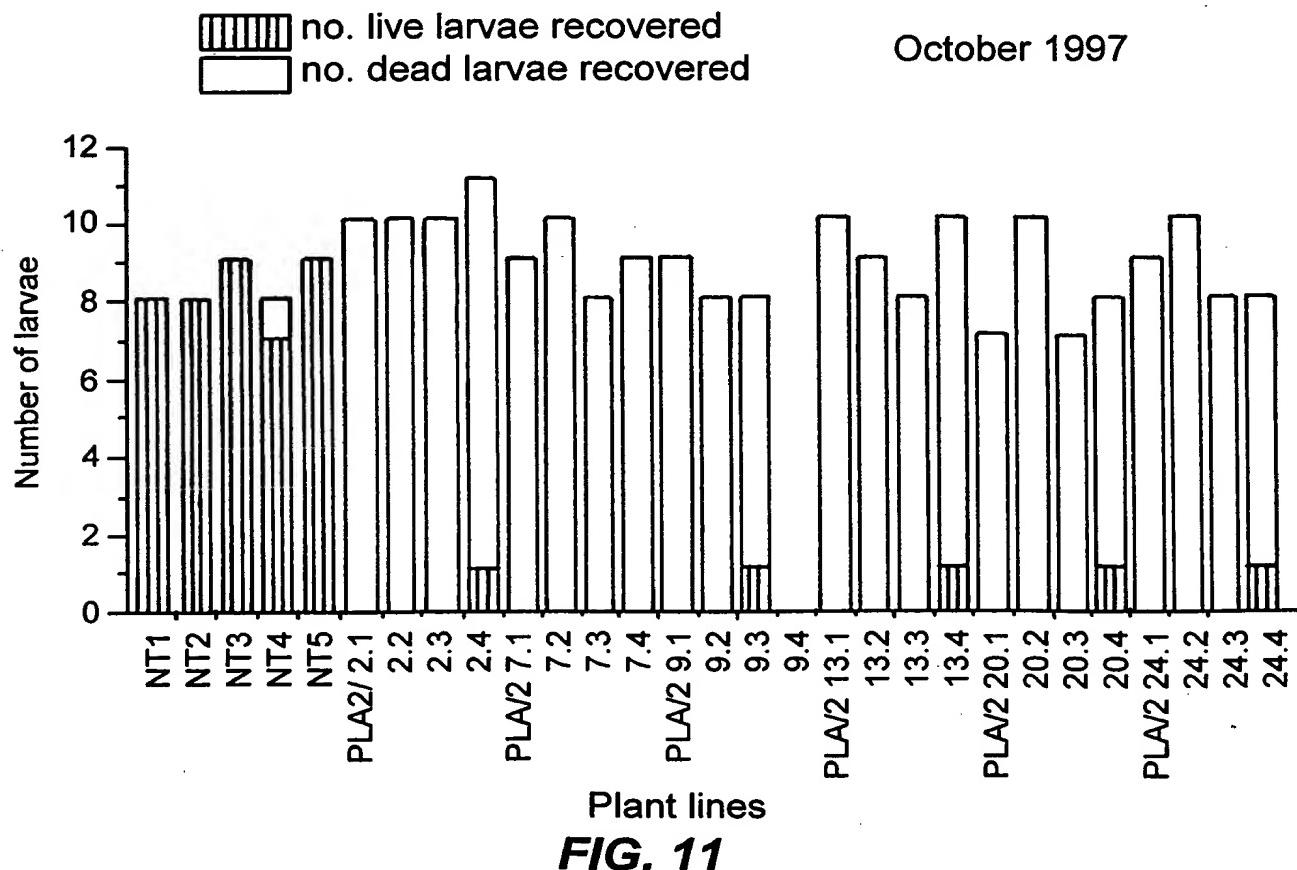


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September 1997



**FIG. 10**



**FIG. 11**



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A)

1 CCCTCCGTCC CCGCCGGCA ACAACTAGGG AGTATTTTC GTGTCTCACA  
51 TGC GCAAGAT CGTCGTTGCA GCCATCGCCG TTTCCCTGAC CACGGTCTCG  
101 ATTACGGCCA GCGCTTCGGC AGACCCCTCC AAGGACTCGA AGGCCAGGT  
151 CTCGGCCGCC GAGGCCGGCA TCACCGGCAC CTGGTACAAC CAGCTCGGCT  
201 CGACCTTCAT CGTGACCGCG GGC GCGCCGACG GCGCCCTGAC CGGAACCTAC  
251 GAGTCGGCCG TCGGCAACGC CGAGAGCCGC TACGT CCTGA CCGGTCGTTA  
301 CGACAGCGCC CCGGCCACCG ACGGCAGCGG CACCGCCCTC GGTTGGACGG  
351 TGGCCTGGAA GAATAACTAC CGCAACGCC ACTCCGCGAC CACGTGGAGC  
401 GGCCAGTACG TCGGCGCGC CGAGGCAGGG ATCAACACCC AGTGGCTGCT  
451 GACCTCCGGC ACCACCGAGG CCAACGCCTG GAAGTCCACG CTGGTCGCCC  
501 ACGACACCTT CACCAAGGTG AAGCCGTCCG CGCCTCCAT CGACGCGCG  
551 AAGAAGGCCG GCGTCAACAA CGGCAACCCG CTCGACGCCG TTCAGCAGTA  
601 GTCGCGTCCC GGCACCGCG GGTGCCGGGA CCTCGGCC

B)

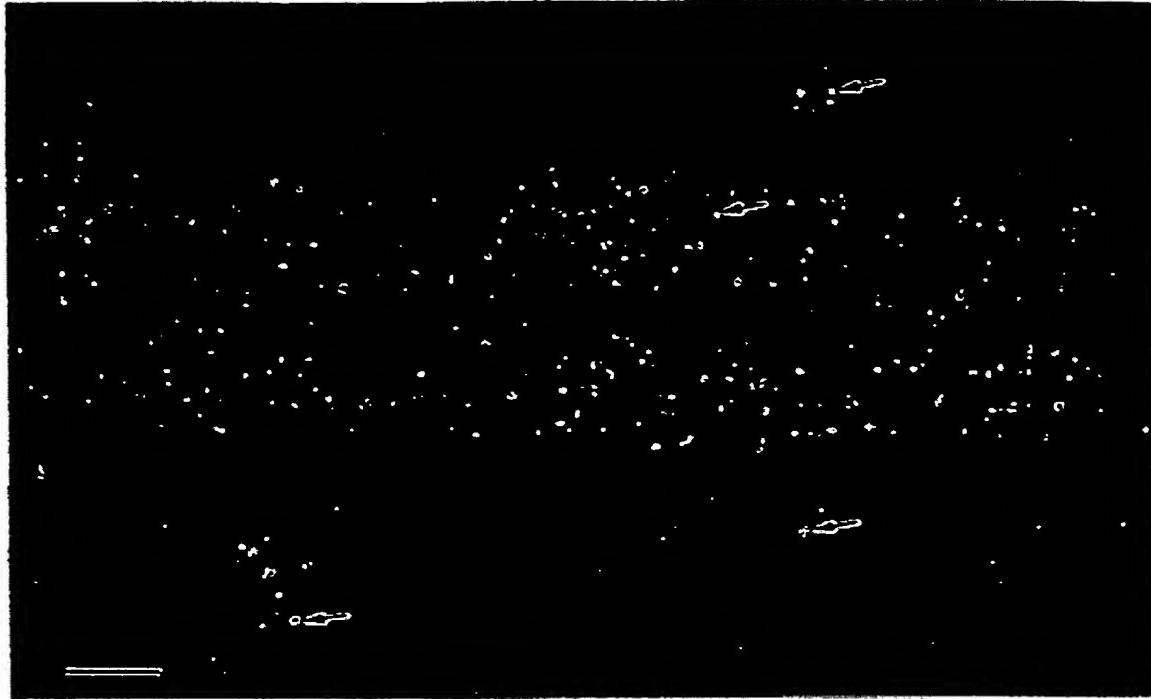
1 MRKIVVAAIA VSLTTVSITA SASADPSKDS KAQSAAEAG ITGTWYNQLG  
51 STFIVTAGAD GAL TGTYESA VGNAESRYVL TGRYDSAPAT DGSGTALGWT  
101 VAWKNNYRNA HSATTWSQY VGGAEARINT QWL LTSGTTE ANAWKSTLVG  
151 HDTFTKVKP S AASIDAAKKA GVNNGNPLDA VQQ

Figure 12

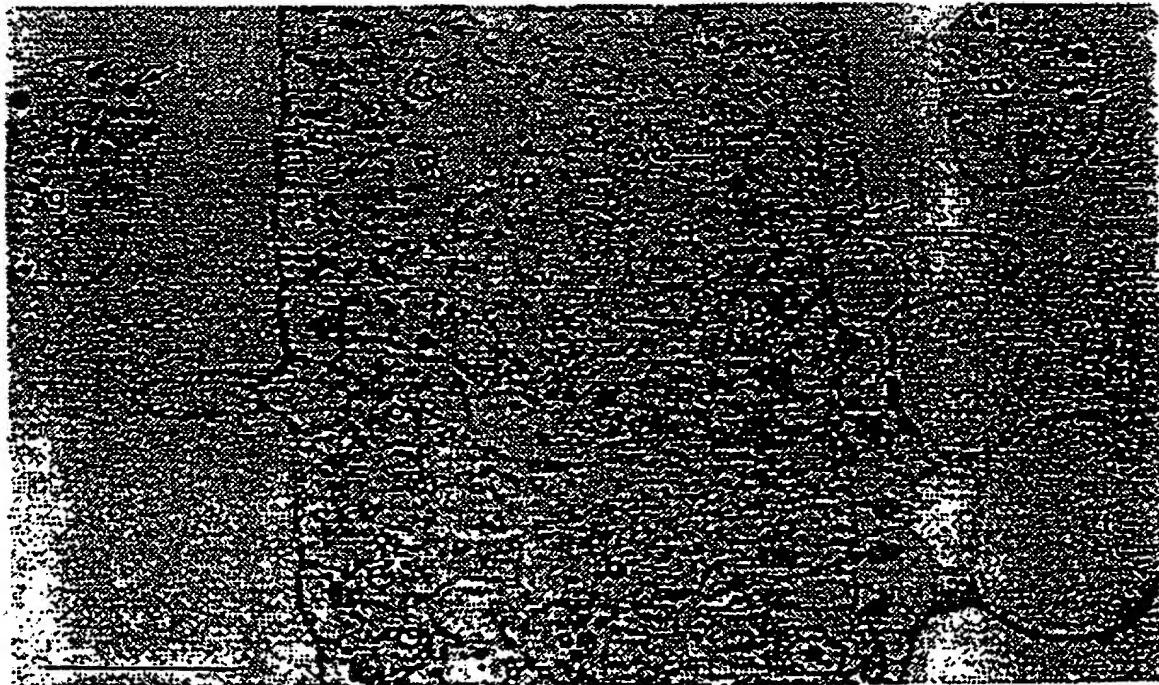


Application Serial No. 09/743,690 - Filed: May 11, 2001  
Inventors: Christeller *et al.* - Attorney Docket No.: 020809-000100US  
Replacement Sheet

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**Figure 13**



**Figure 14**

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Figure 15

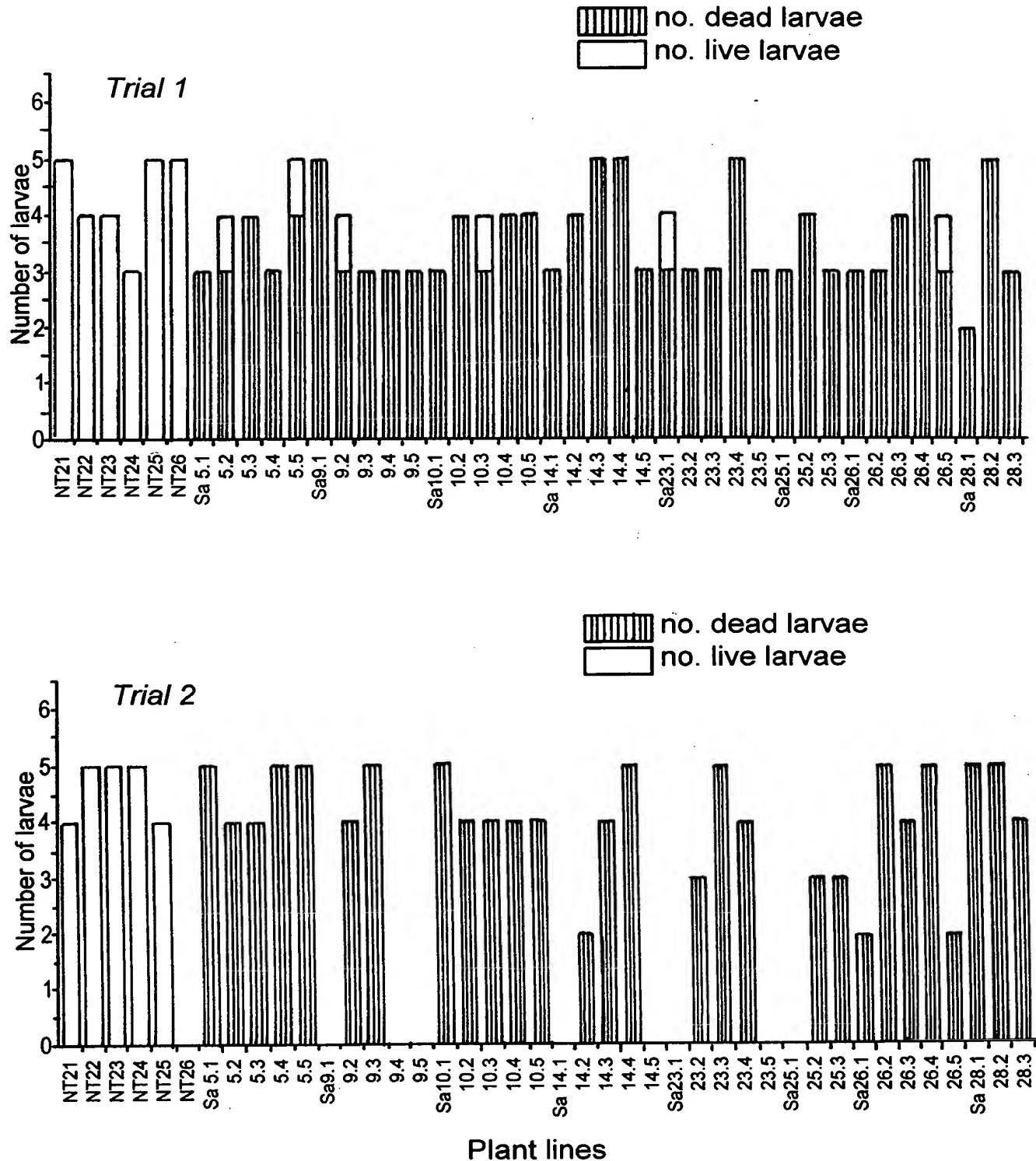


Figure 16

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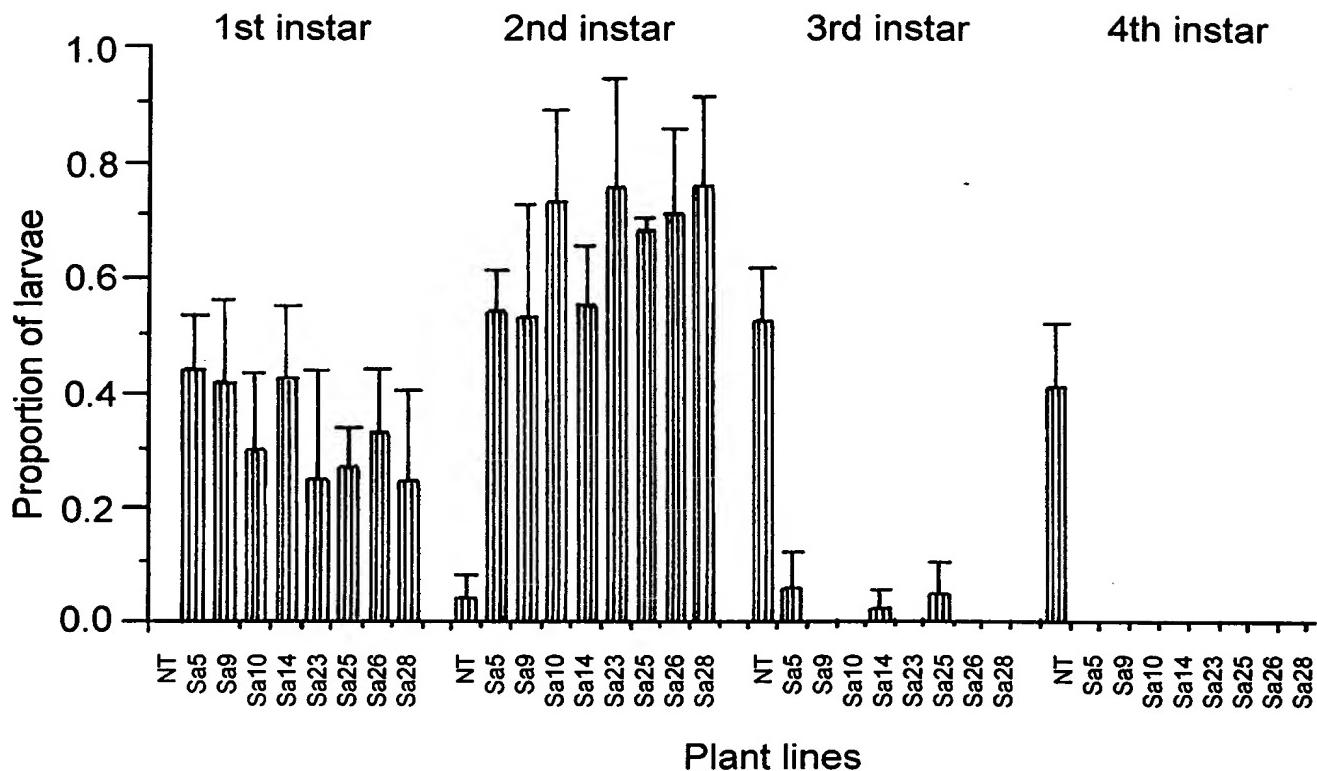
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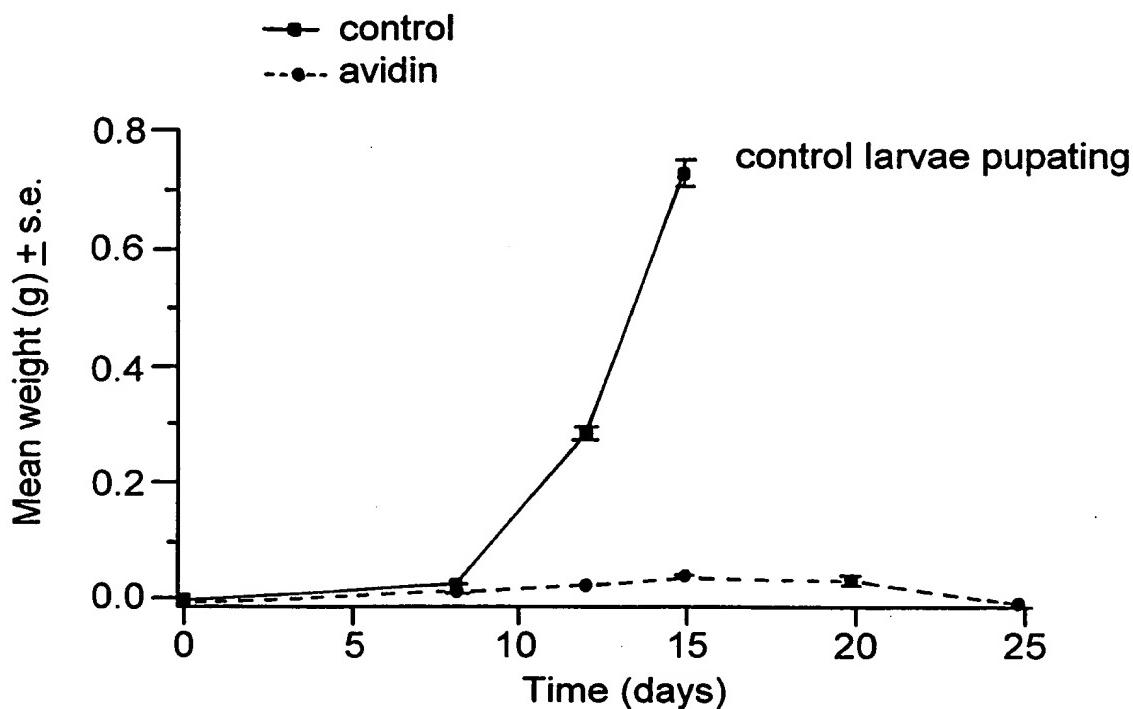
**FIG. 17**



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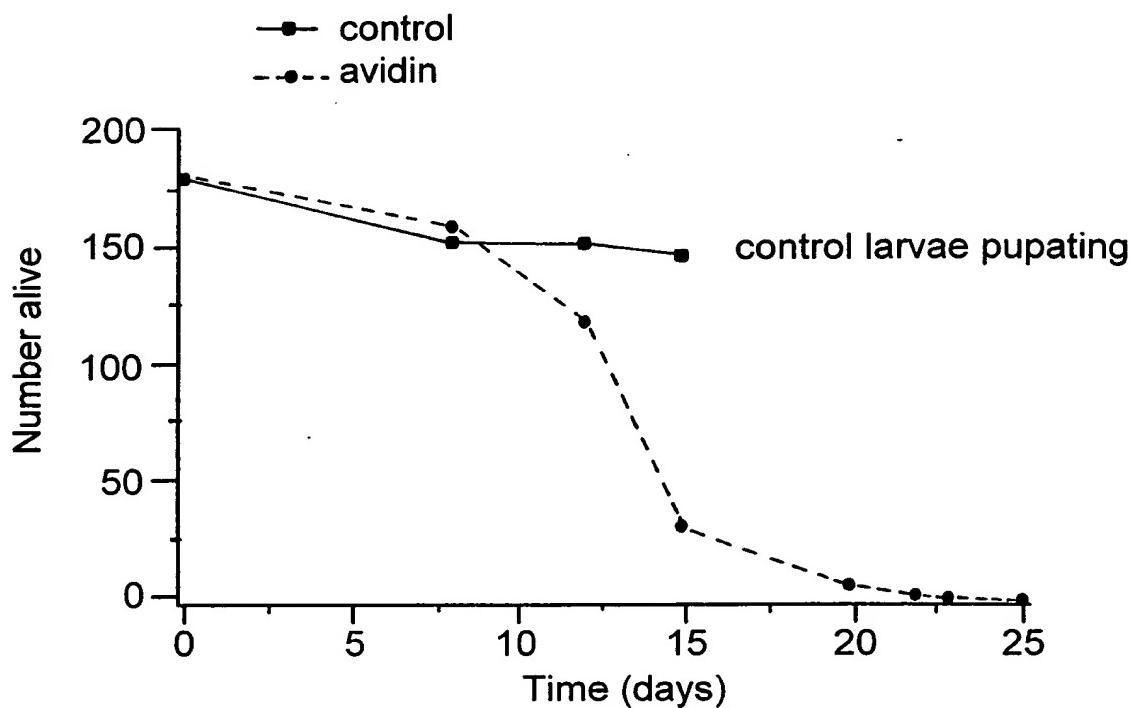
**FIG. 18**



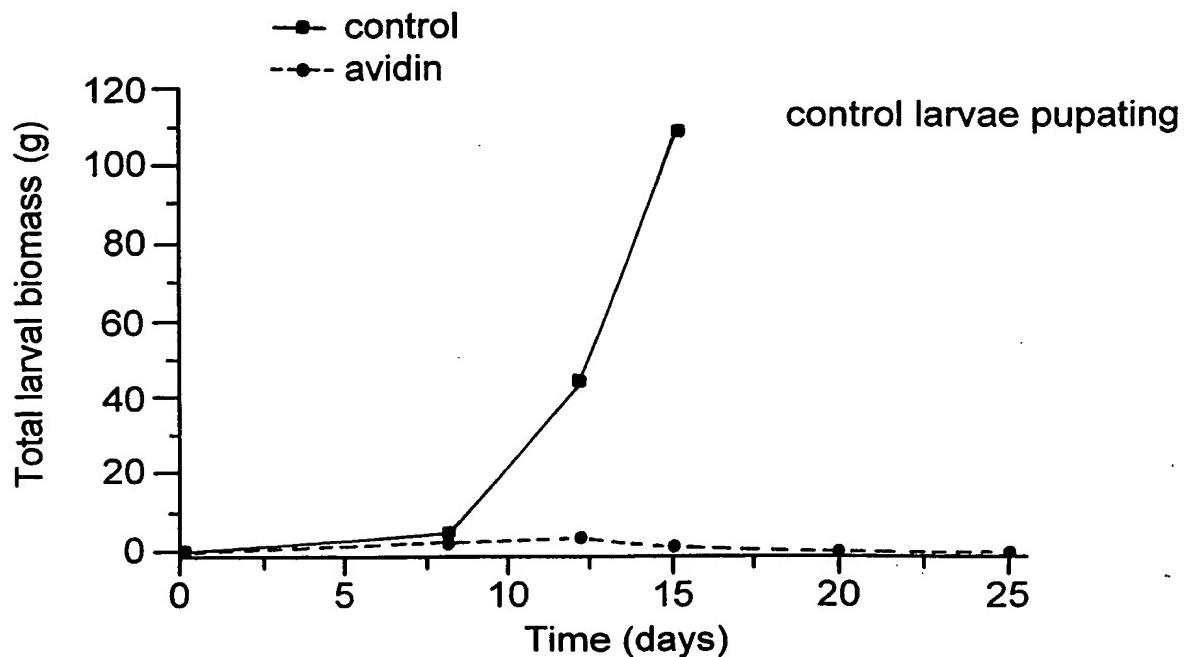
**FIG. 19**

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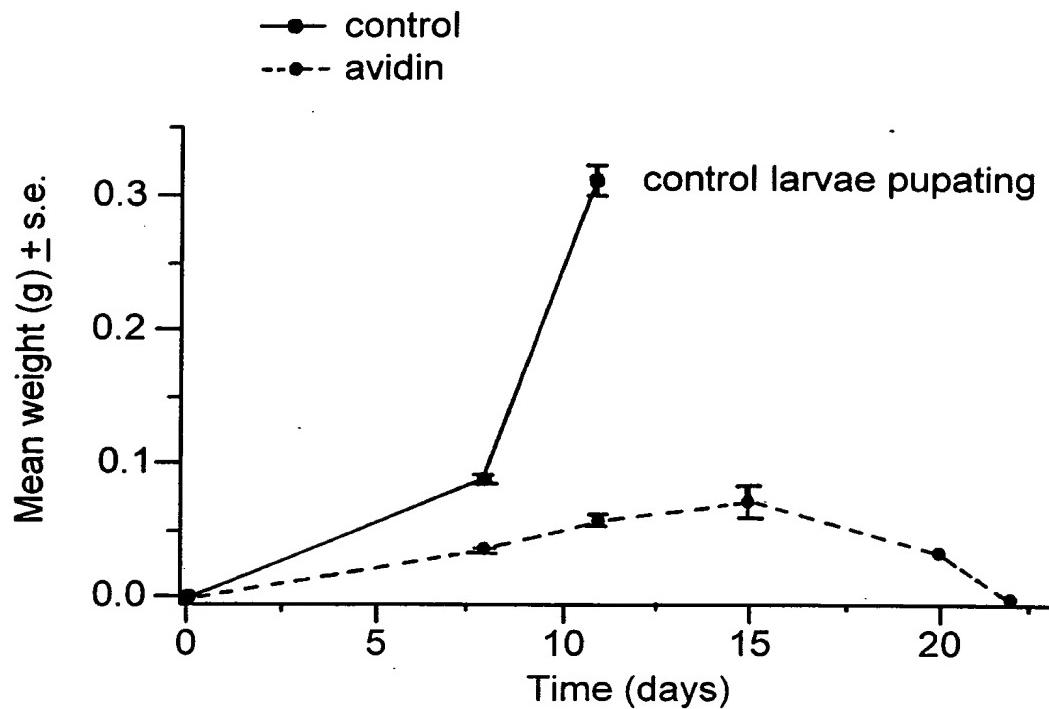
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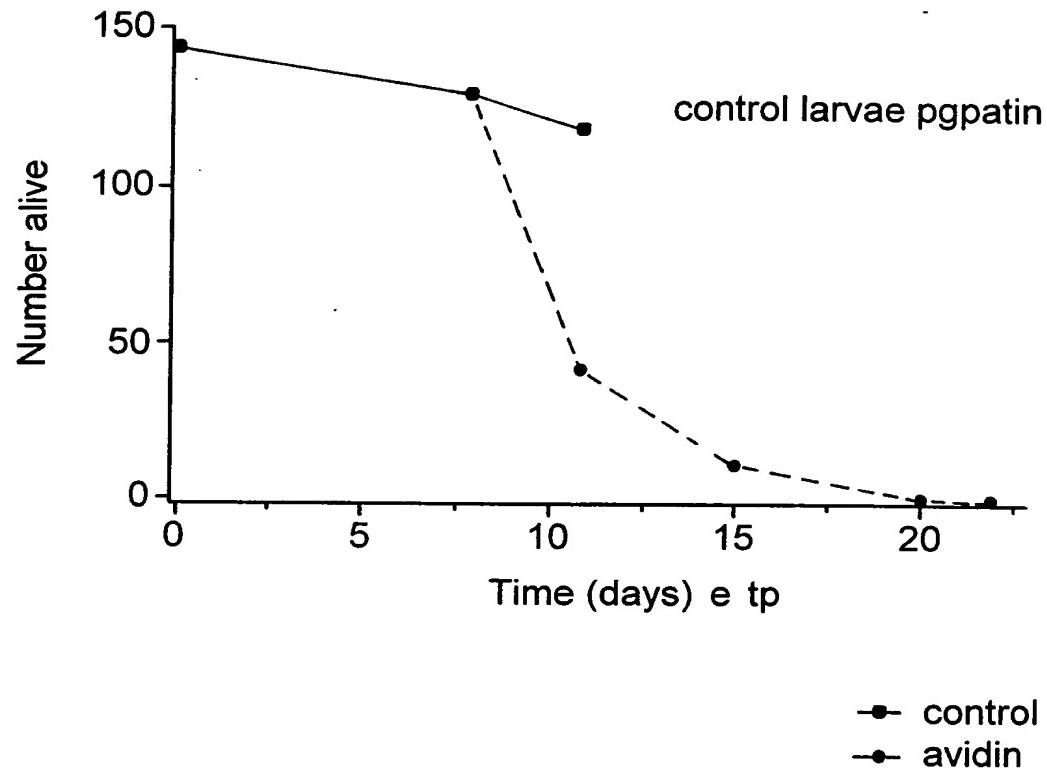
**FIG. 20**



**FIG. 21**



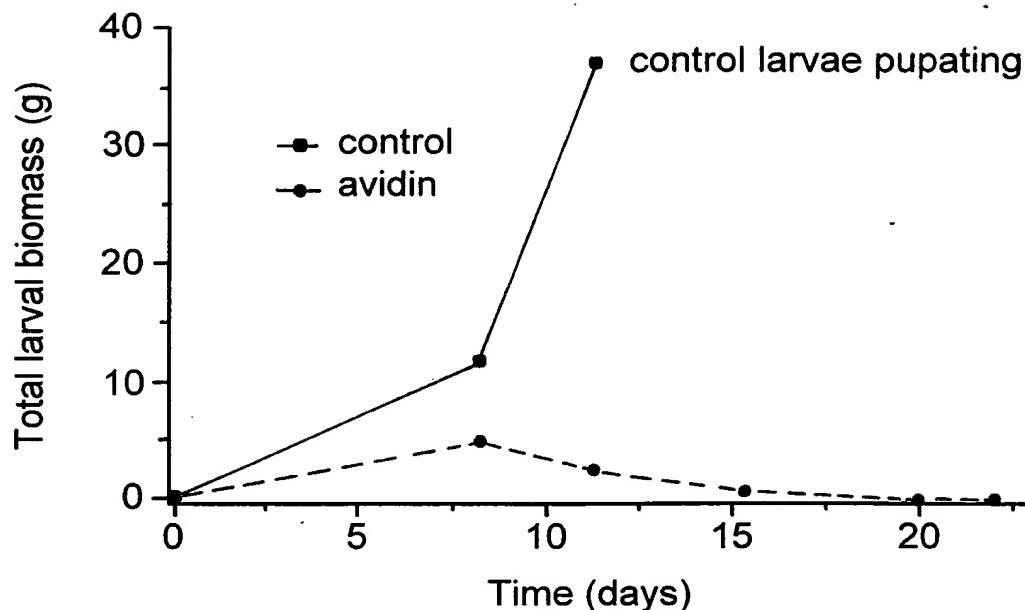
**FIG. 22**



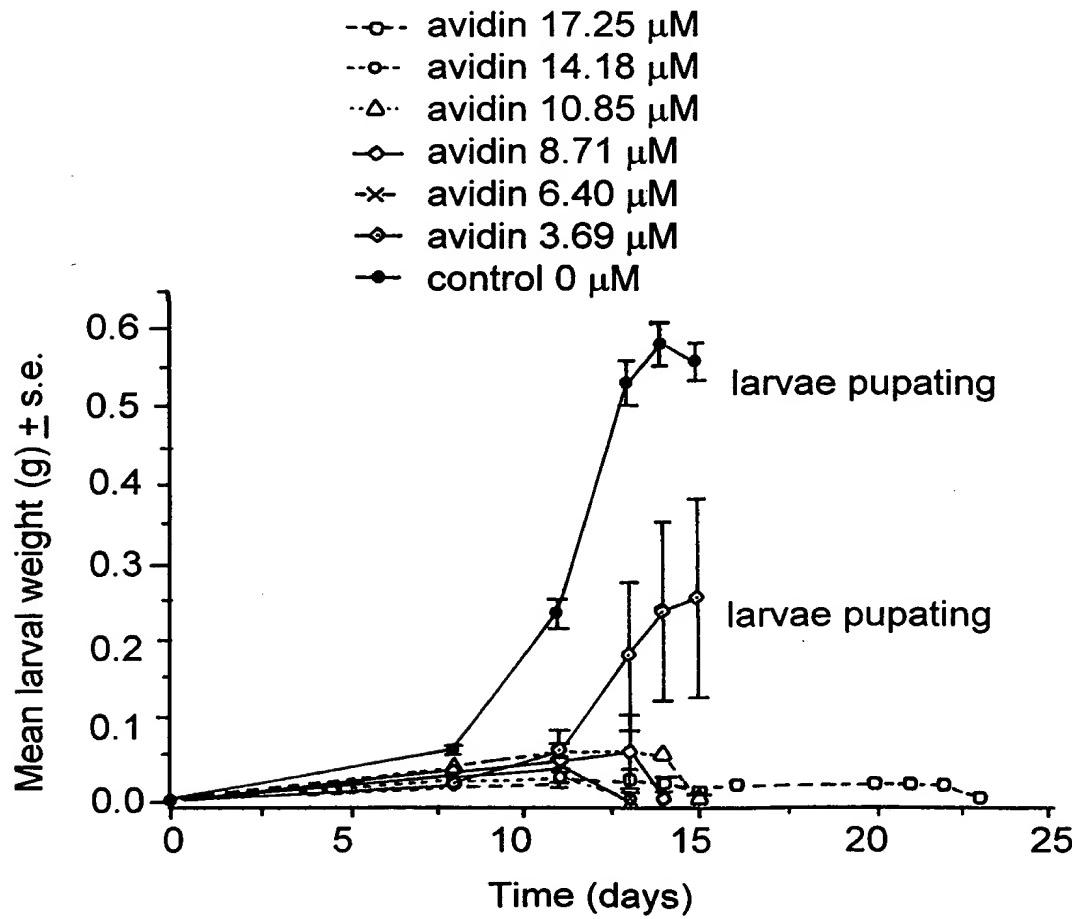
**FIG. 23**

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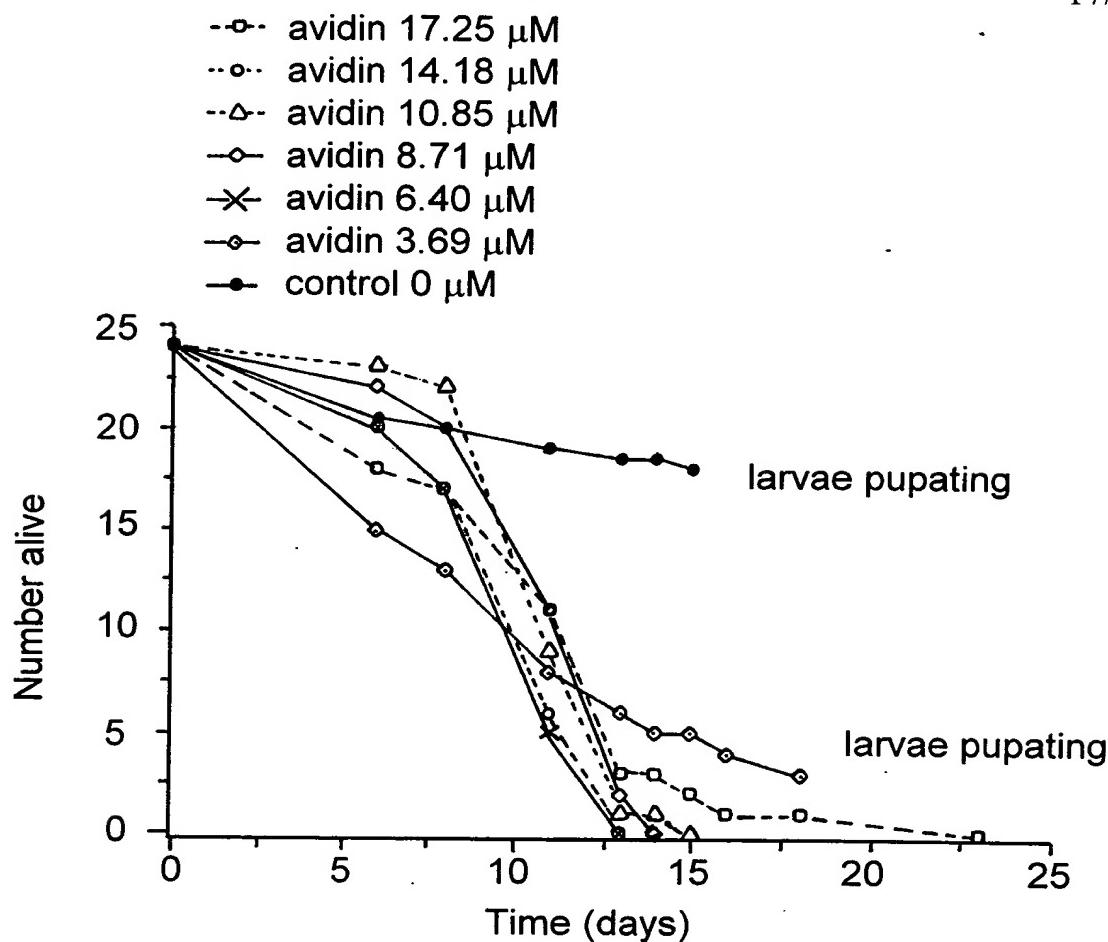
**FIG. 24**



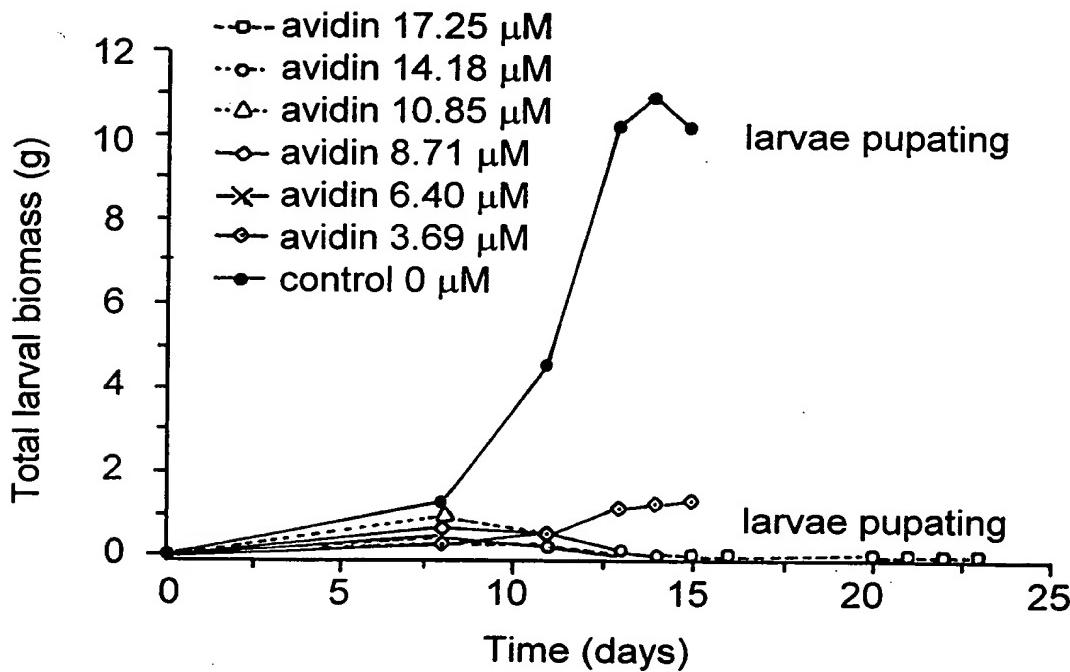
**FIG. 25**

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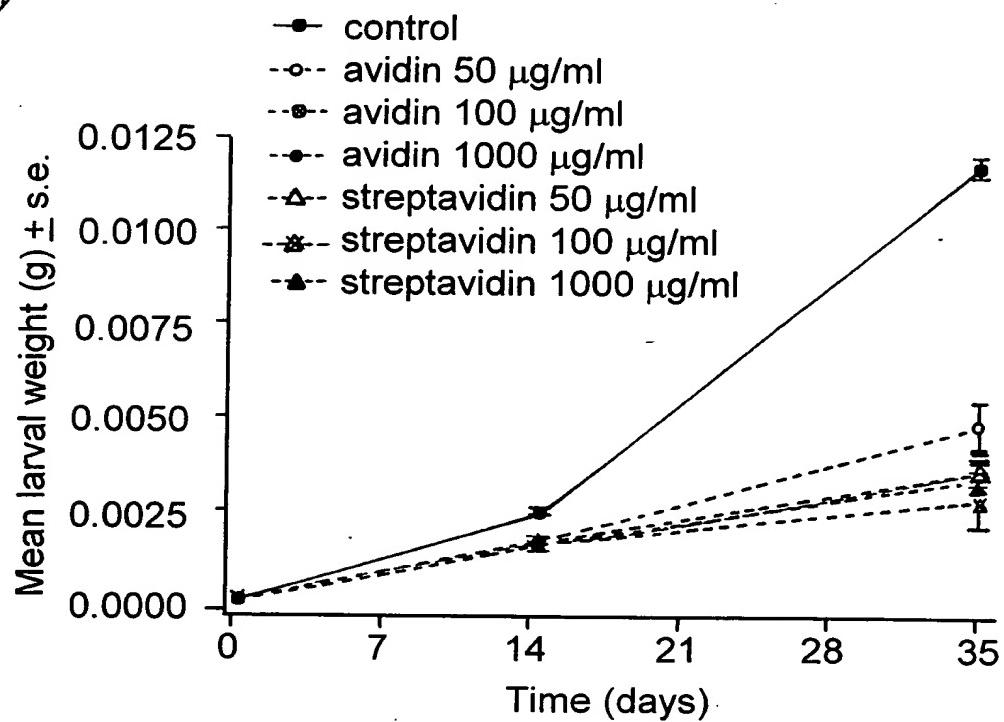
**FIG. 26**



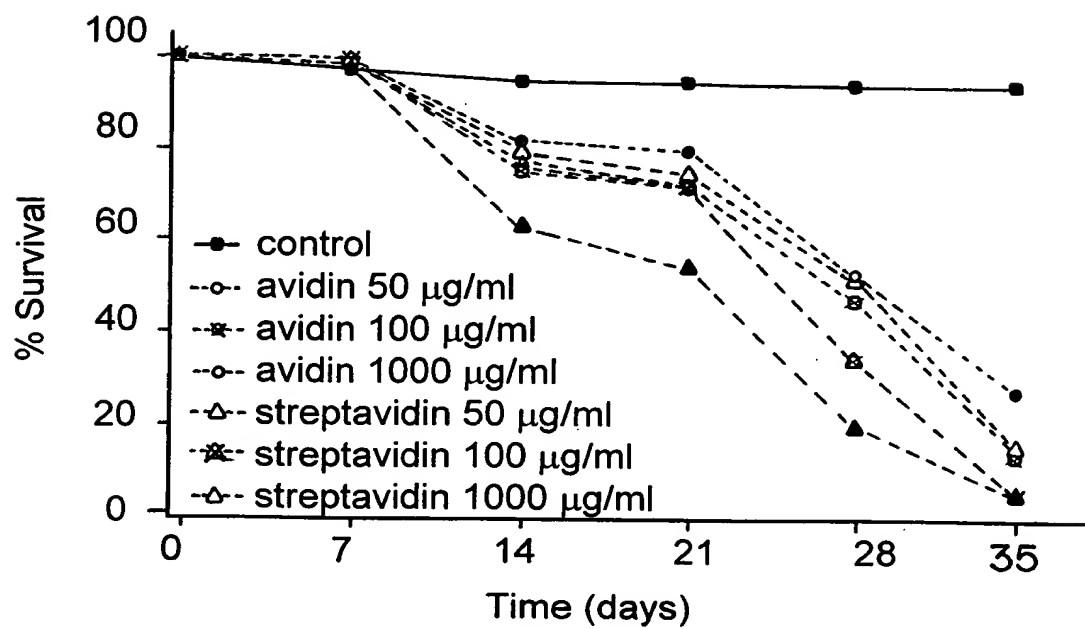
**FIG. 27**

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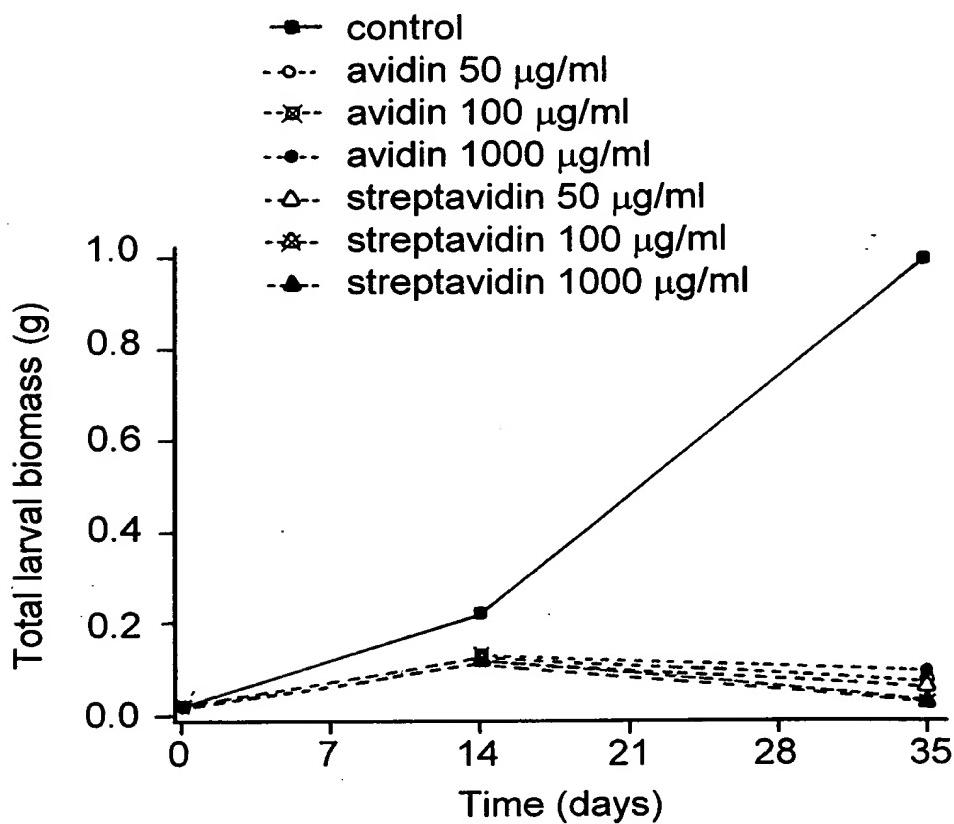
**FIG. 28**



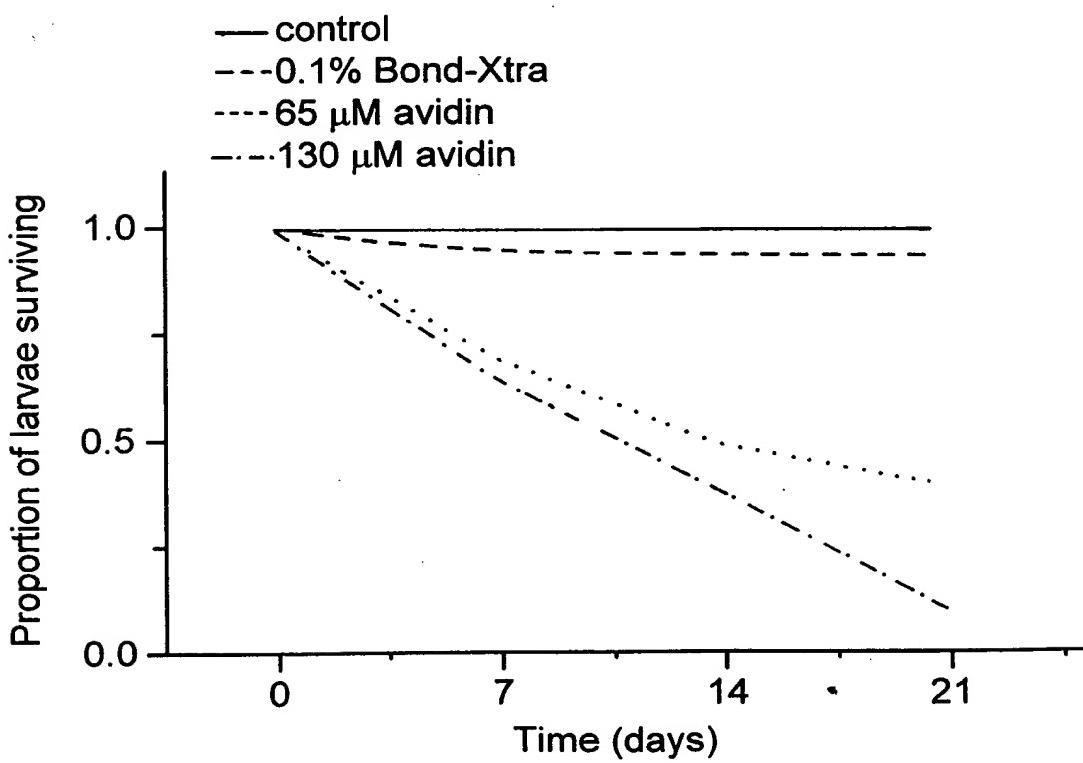
**FIG. 29**

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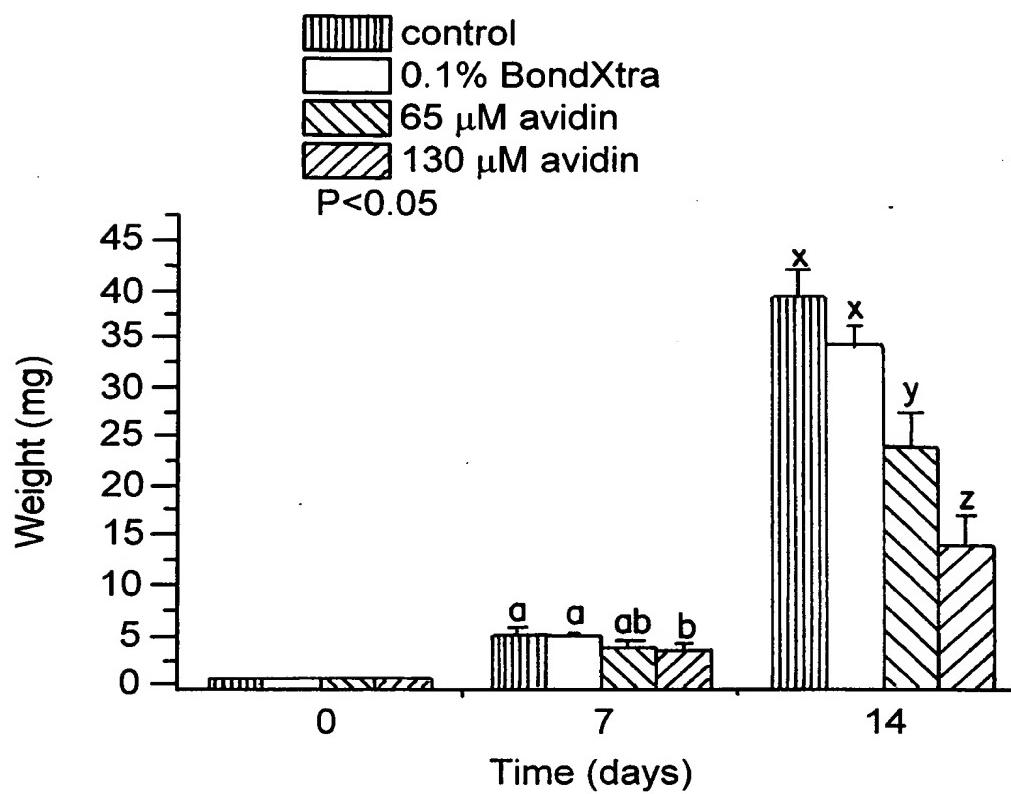
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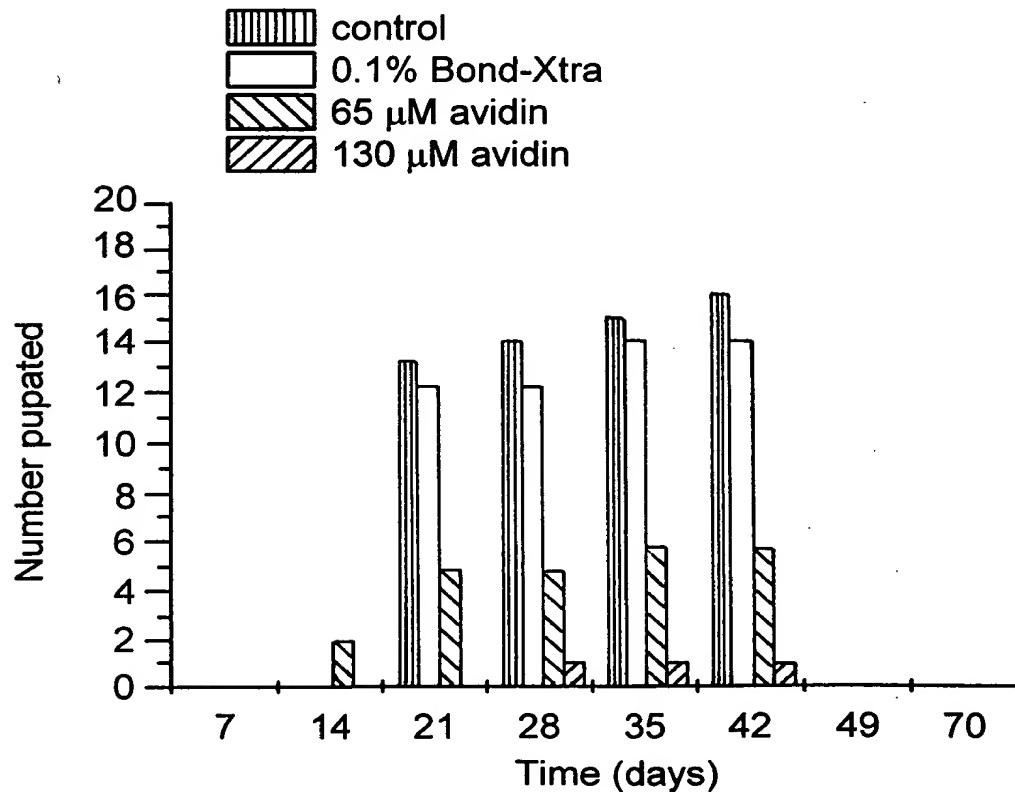
**FIG. 30**



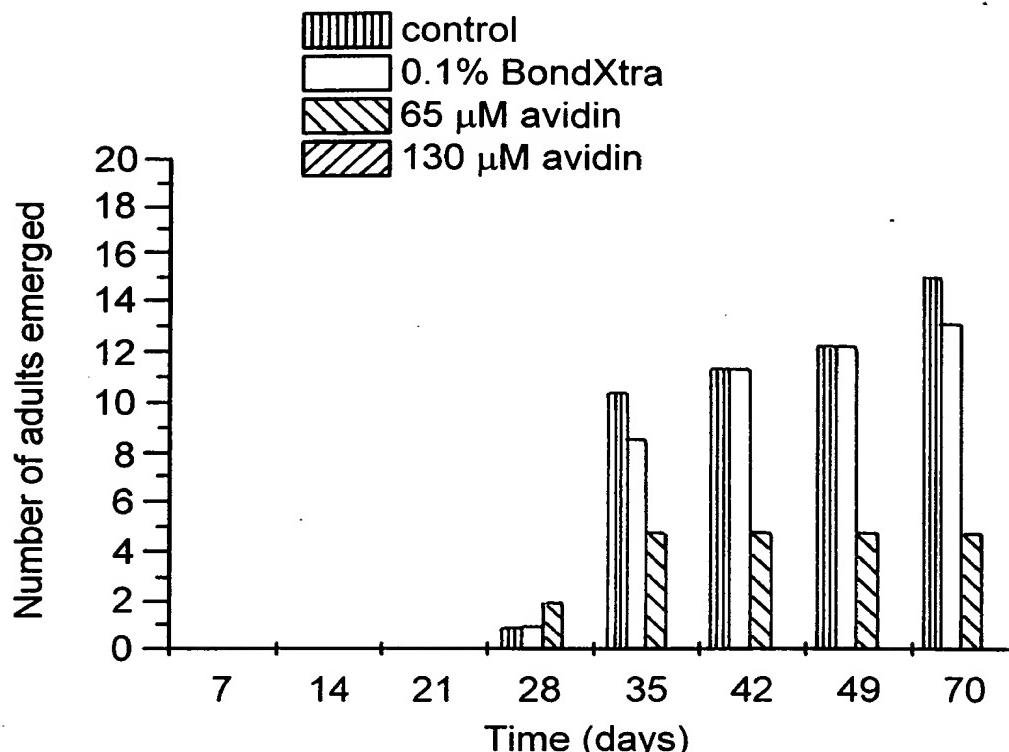
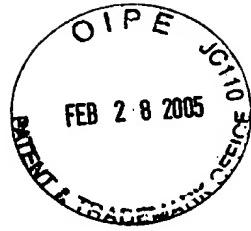
**FIG. 31**



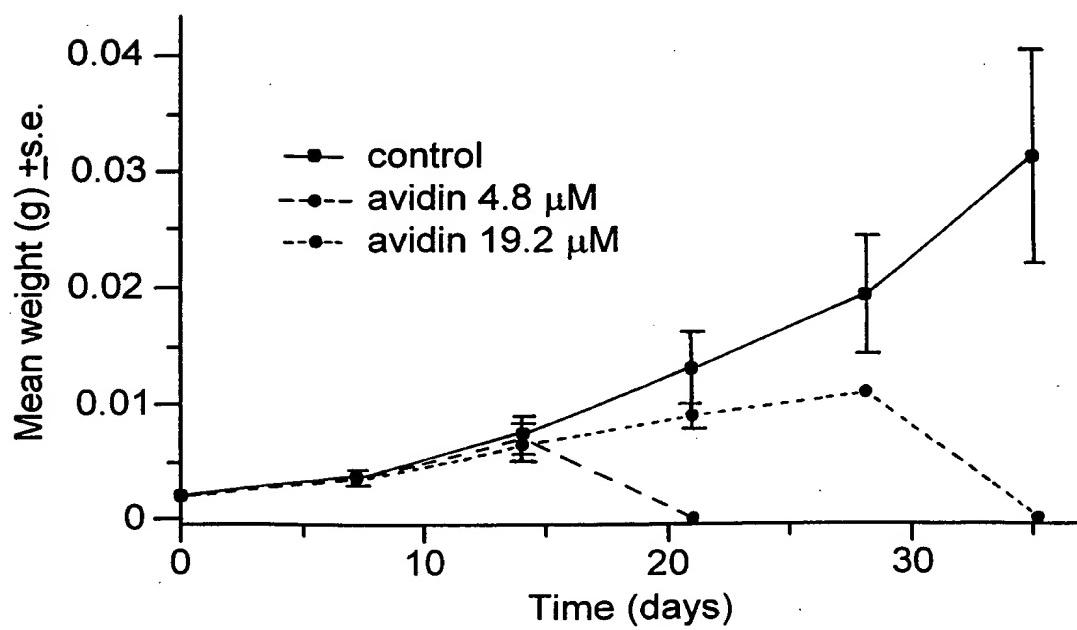
**FIG. 32**



**FIG. 33**



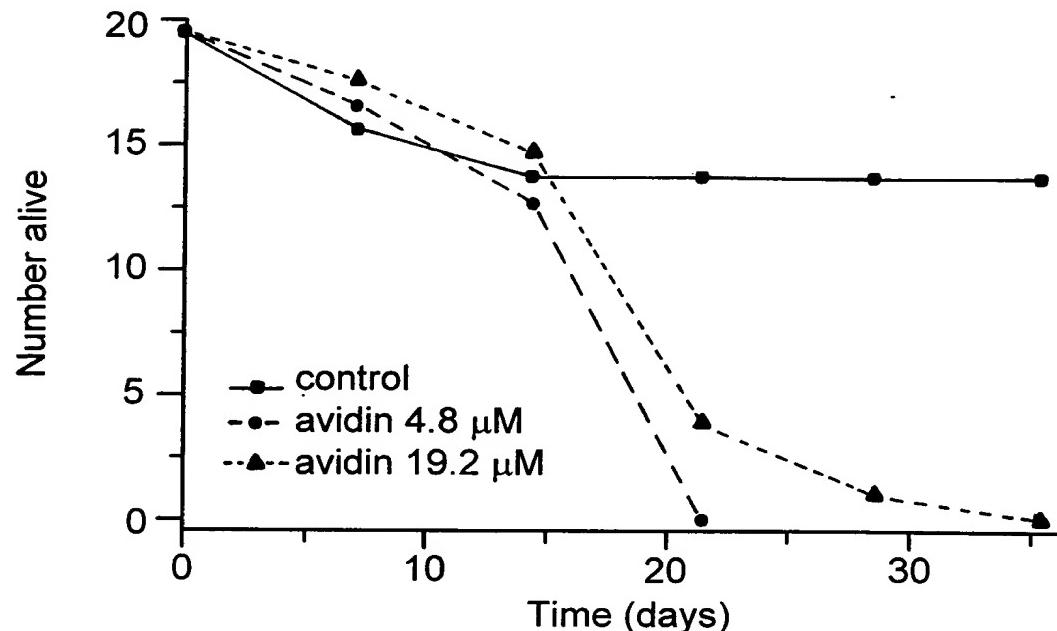
**FIG. 34**



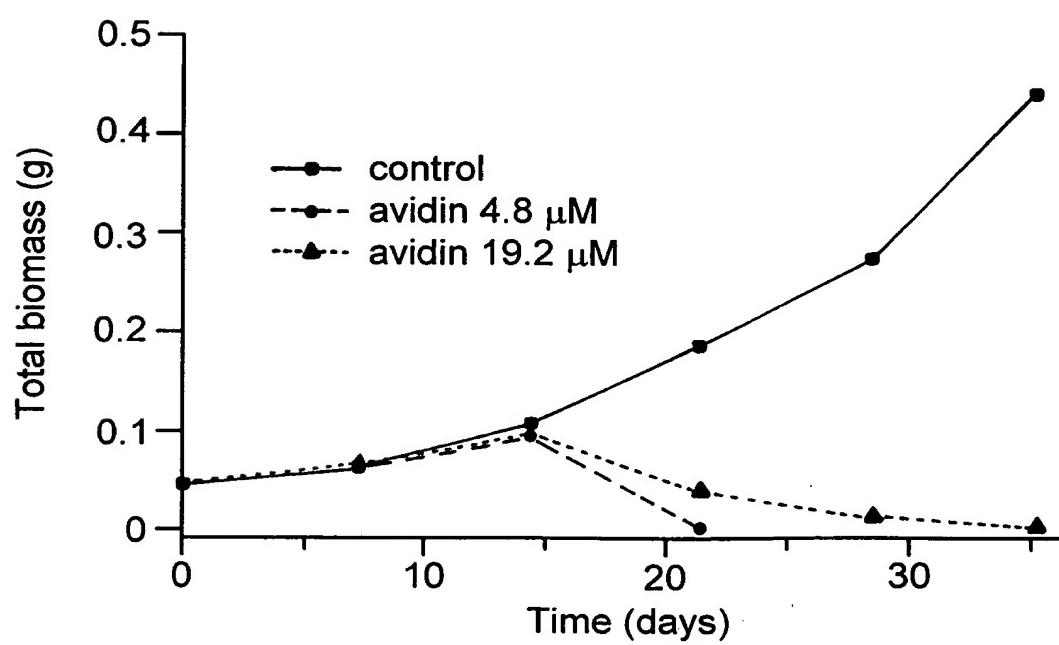
**FIG. 35**

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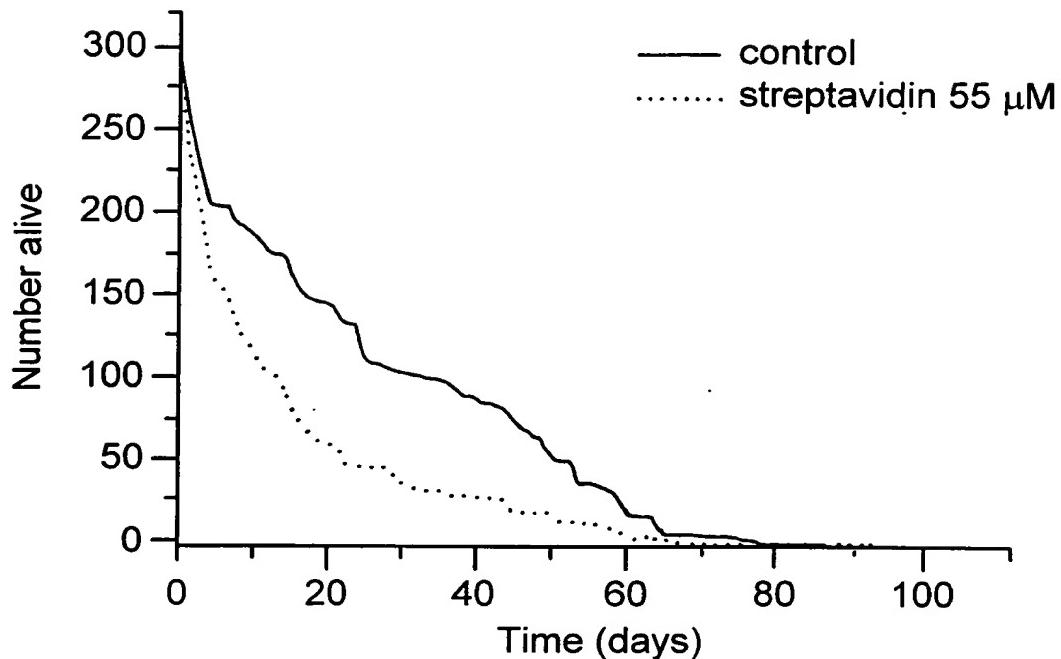
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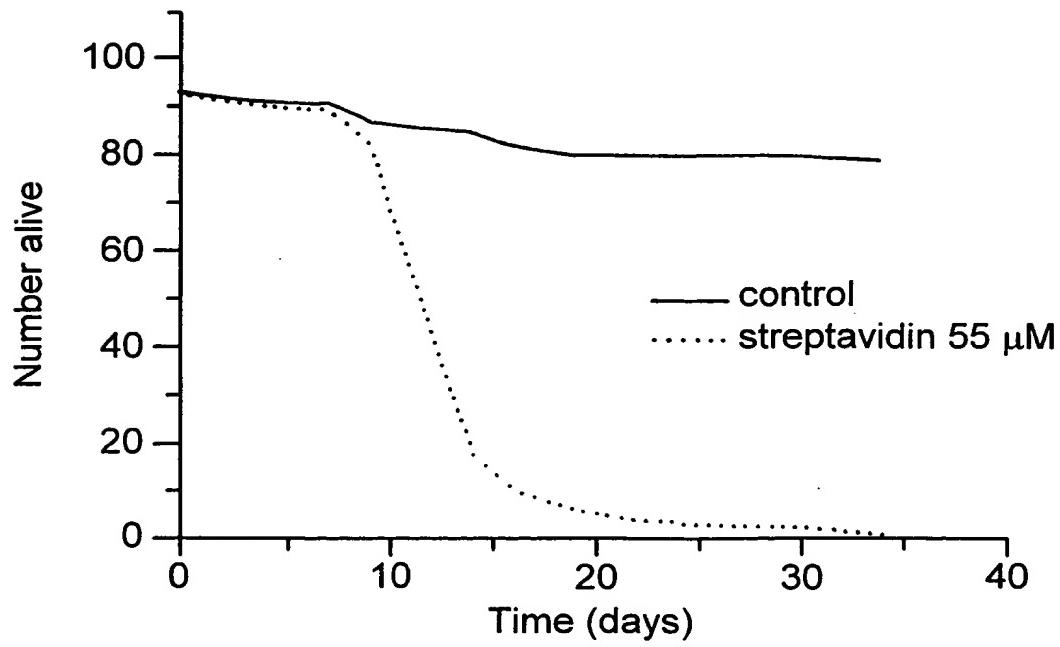
**FIG. 36**



**FIG. 37**



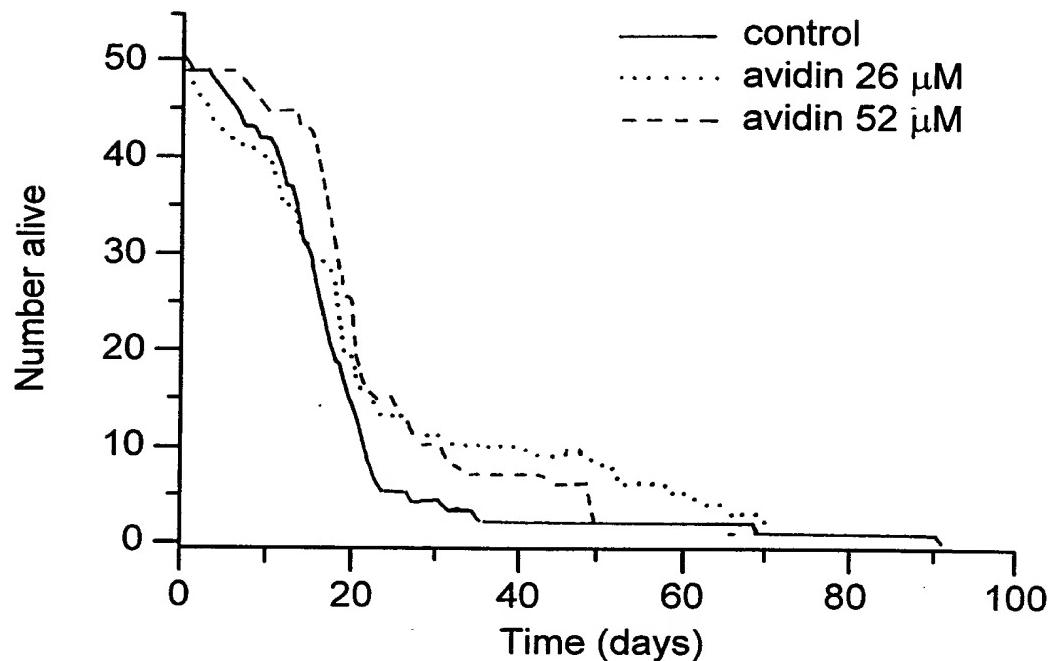
**FIG. 38**



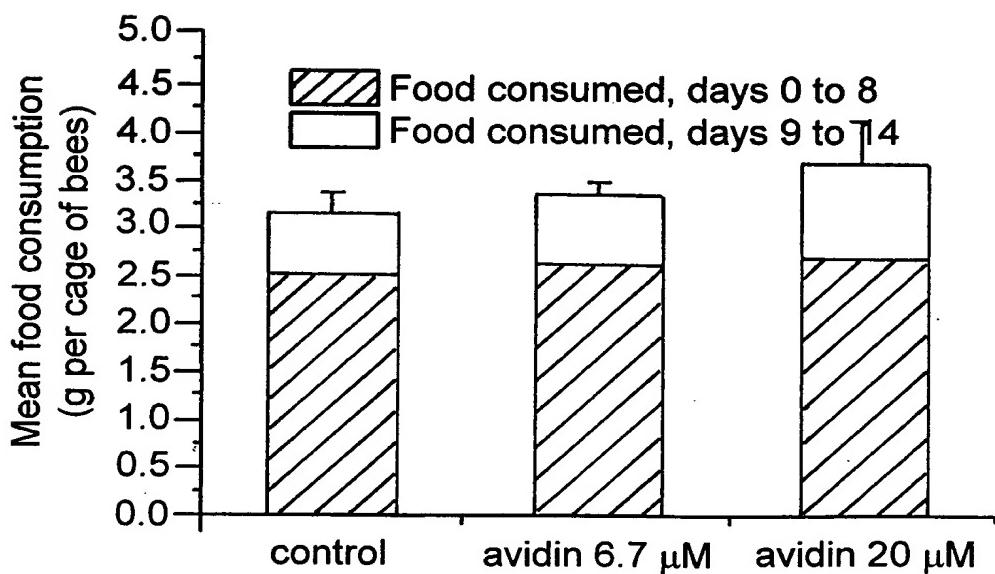
**FIG. 39**

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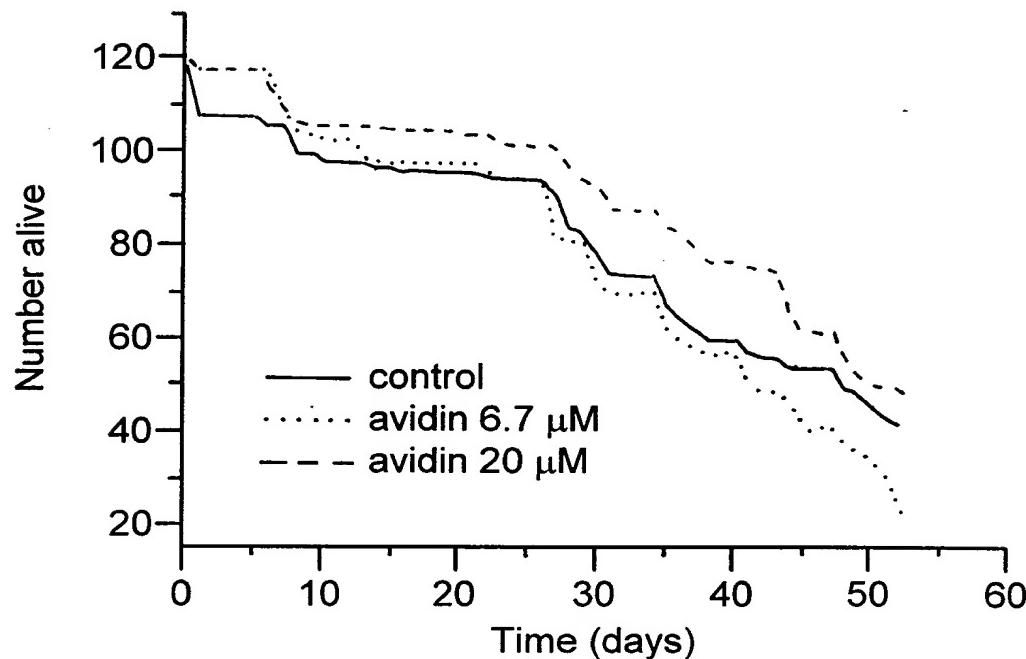
**FIG. 40**



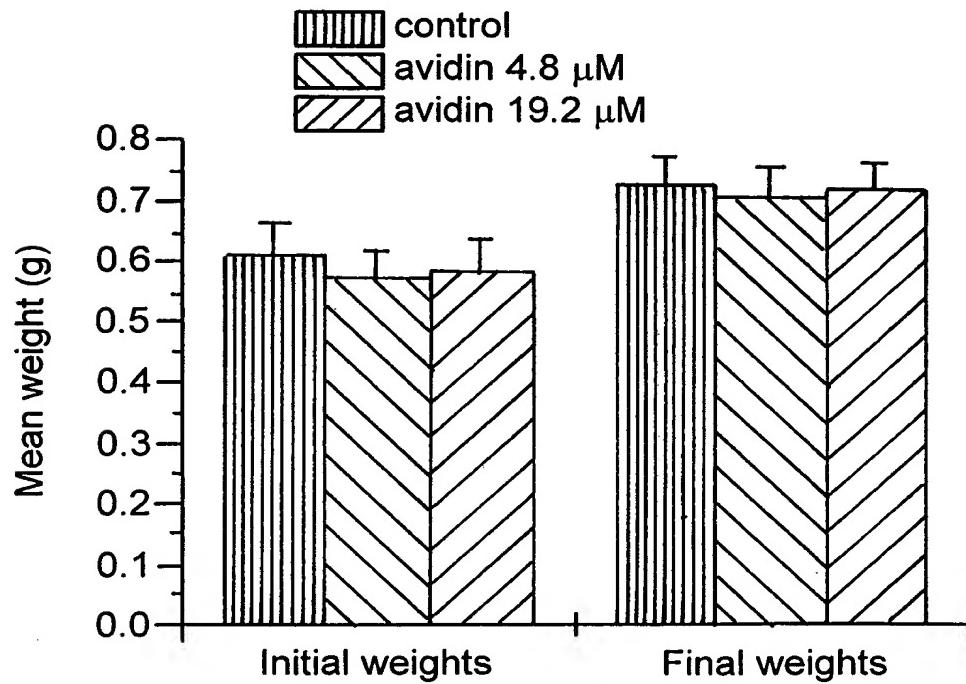
**FIG. 41**

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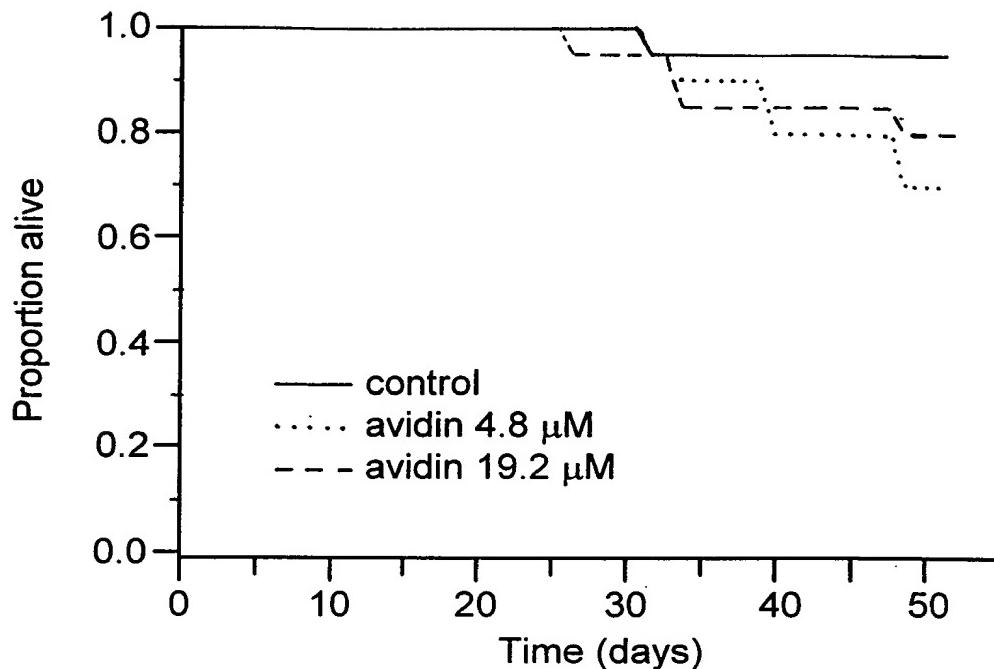
**FIG. 42**



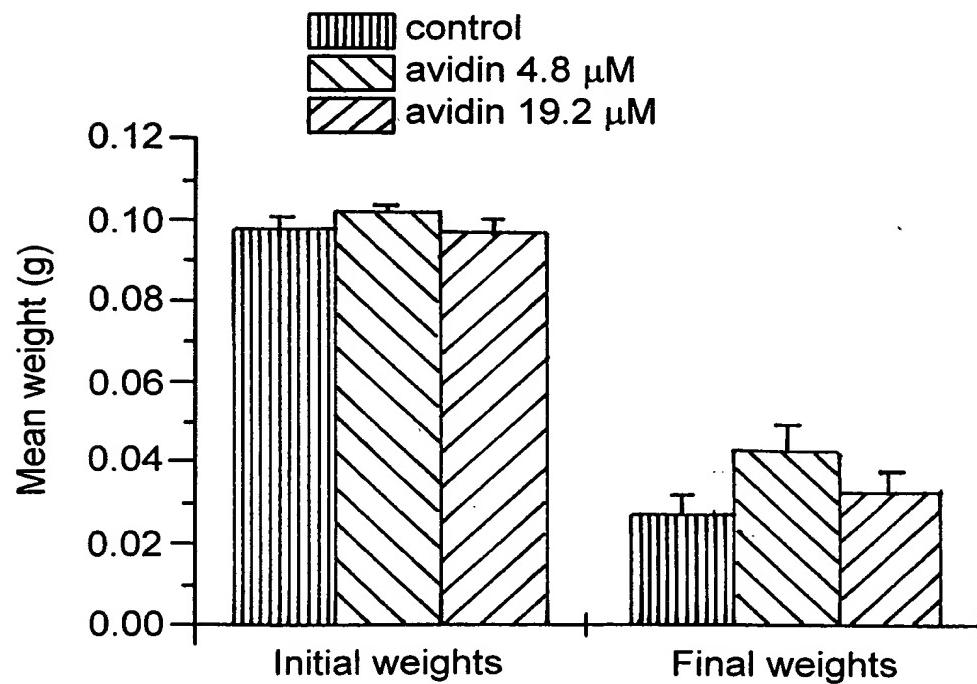
**FIG. 43**

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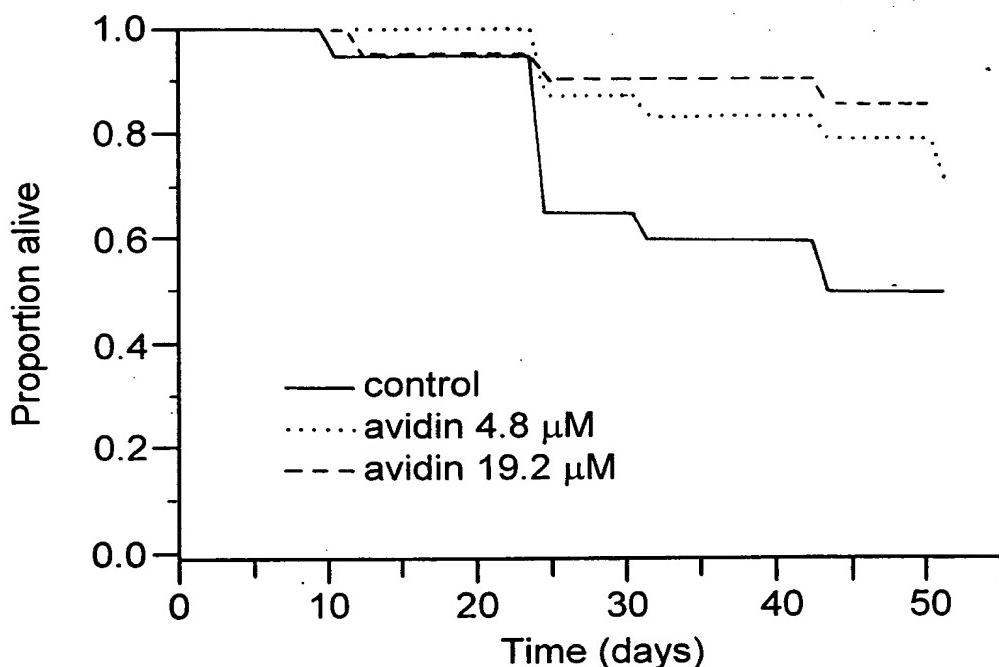
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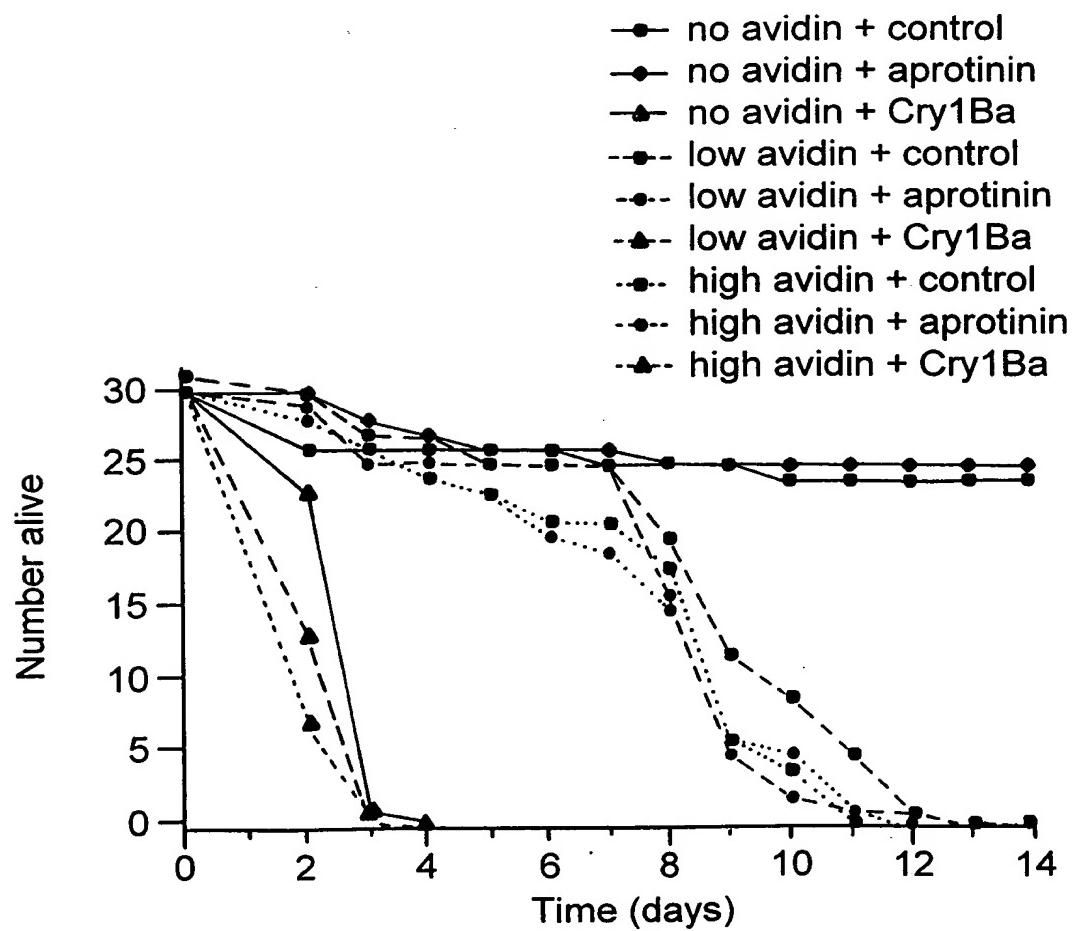
**FIG. 44**



**FIG. 45**



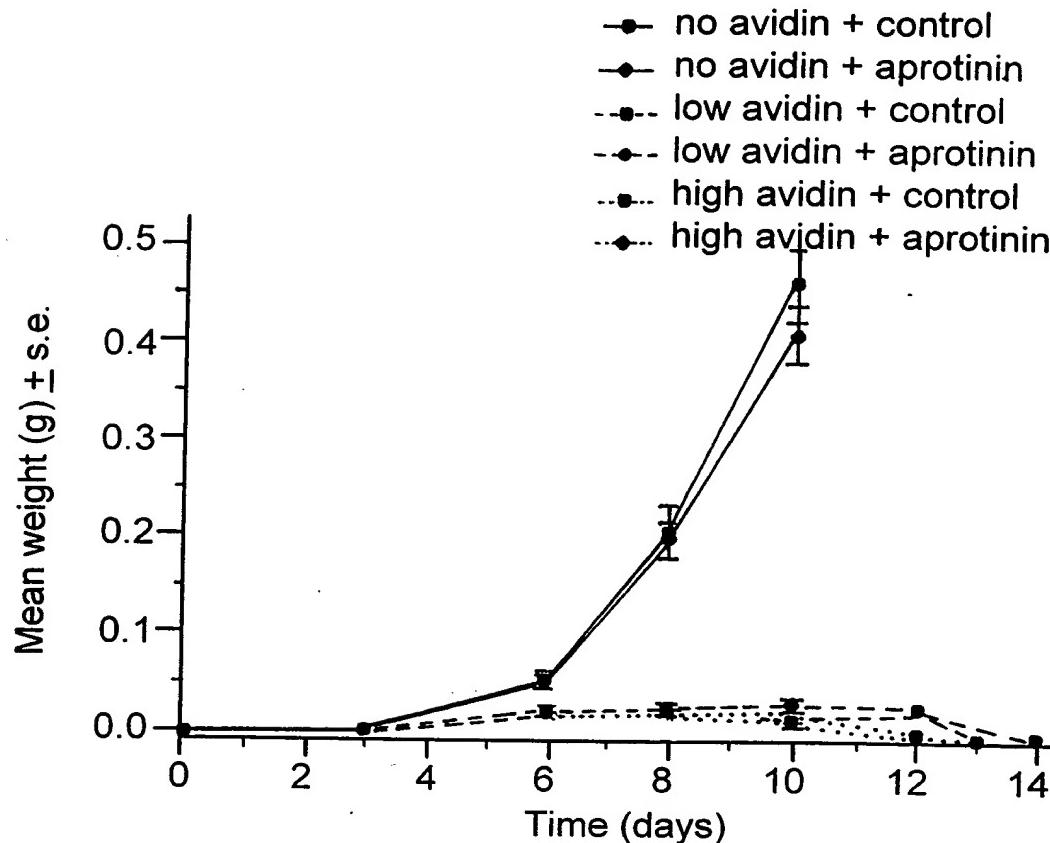
**FIG. 46**



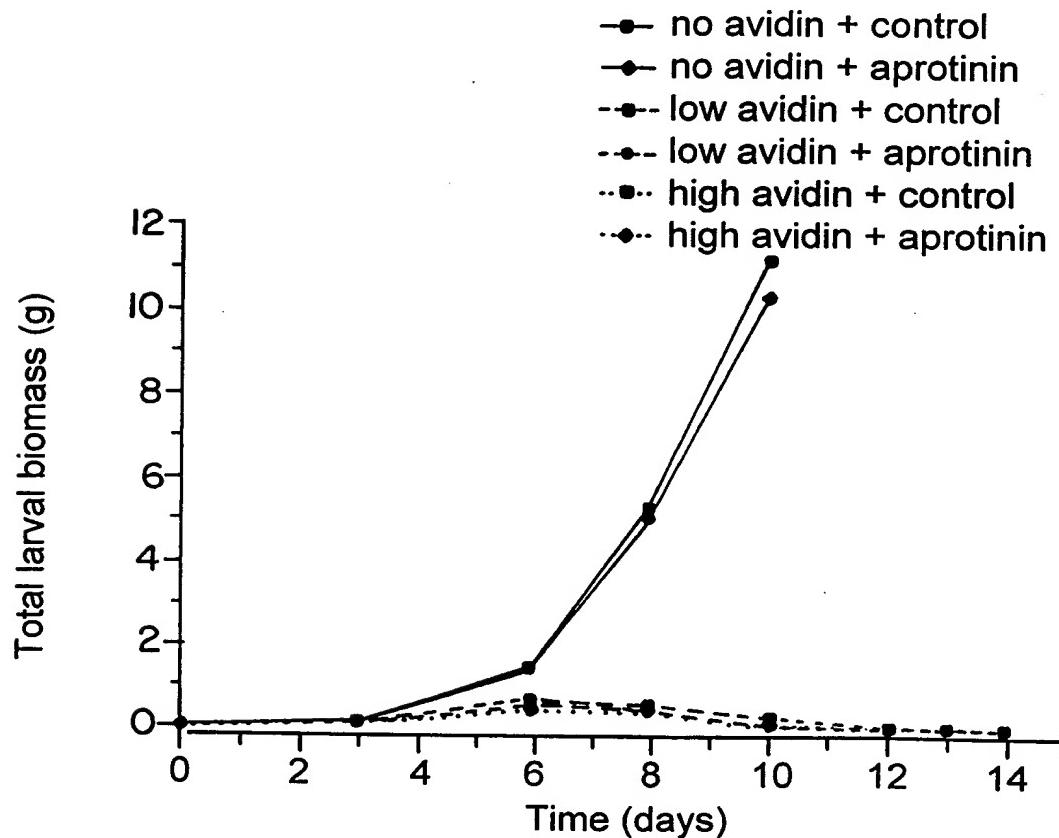
**FIG. 47**

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**FIG. 48**



**FIG. 49**